# IMMUNIZATION AND PREVENTIVE MEDICINE, 1982

## HEARING

BEFORE THE

## SUBCOMMITTEE ON INVESTIGATIONS AND GENERAL OVERSIGHT

OF THE

## COMMITTEE ON LABOR AND HUMAN RESOURCES UNITED STATES SENATE

NINETY-SEVENTH CONGRESS

SECOND SESSION

ON

TO EXAMINE ADVERSE DRUG REACTIONS FROM IMMUNIZATION, FEDERAL EFFORTS IN PREVENTIVE MEDICINE, AND CHARACTERISTICS OF CERTAIN DISEASES

MAY 7, 1982

Printed for the use of the Committee on Labor and Human Resources

U.S. GOVERNMENT PRINTING OFFICE

96-132 O WASHINGTON: 1982

554-62

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# IMMUNIZATION AND PREVENTIVE MEDICINE, 1982

FRIDAY, MAY 7, 1982

U.S. SENATE,
SUBCOMMITTEE ON INVESTIGATIONS
AND GENERAL OVERSIGHT,
COMMITTEE ON LABOR AND HUMAN RESOURCES,
*Washington, D.C.*

The subcommittee convened, pursuant to notice, at 10 a.m., in room 4232, Dirksen Senate Office Building, Senator Paula Hawkins (chairman of the subcommittee) presiding.

Present: Senator Hawkins.

Staff present: Jay Howell, chief counsel; Terri Parker, counsel; Tim Jenkins and Lisa Demetree, staff investigators; and Walter Sheridan, minority professional staff.

## OPENING STATEMENT OF SENATOR HAWKINS

Senator HAWKINS. Good morning. It is 10 o'clock, the time that has been set for this hearing. Senator Kennedy has notified me he will be with us at 10:30, but we will proceed in the interest of keeping on schedule.

We welcome you all to this oversight hearing on the childhood immunization program and preventive medicine. Today we are going to discuss the current status of the immunization program and its future direction. We will also examine issues of concern and controversy surrounding this vital program and attempt to set the record straight.

Thanks to strong Federal involvement in immunization programs, this country has seen a dramatic decline in the prevalence of seven preventable childhood diseases: polio, measles, rubella, diphtheria, tetanus, pertussis, and mumps. The Federal Government has furnished financial and other assistance to State and local health agencies and allowed them to buy Government-procured vaccines at a discount. This high level of cooperation between the States and Federal Government has resulted in protection against diseases that produce deformity, disability, and death.

The immunization program is a proven method of safeguarding our children against pain, suffering, and death. Although savings in human costs cannot be quantified in dollars, economic considerations alone justify support of the program as a continuing element of Federal public policy. Cost savings from prevention of infectious and crippling diseases include not only the direct costs of physician

care and hospitalization, but also the time and productivity lost from school and work.

The basic soundness and success of the immunization program has been widely demonstrated. A polio outbreak in 1952, which struck 58,000 Americans, caused 14,000 deaths and left thousands of others confined to wheelchairs and steel braces for life. Today, due to the development and availability of the antipolio vaccine, this crippling disease has been all but wiped out in the United States.

Similarly, in the early 1960's, about 400,000 cases of measles were reported in the United States each year. Indeed, measles were so common that they were regarded as an inevitability of childhood despite the danger the disease poses to a child's life and health. I remember sitting in darkened rooms because you were not supposed to be exposed to light. The whole family had the measles, and we hung together while the last child had his, before we were allowed out and could be called noncontagious.

Of 100,000 cases of measles, 10 will result in death, and 100 will result in measles encephalitis. One-third of those 100 will experience permanent mental retardation or other damage to the central nervous system. Some number of cases will also result in blindness, deafness, or other impairments.

Introduction of the measles vaccine during the sixties resulted in a dramatic reduction in the number of reported cases and led to a national campaign to eradicate measles in the United States by October 1982. According to the Center for Disease Control, if the current level of effort can be maintained, it is likely that the United States will soon eliminate this scourge, which is the leading cause of death in some developing countries, killing 1,500,000 children a year.

Trend data on immunizations also shows success against diphtheria, pertussis, mumps, and rubella. A strong immunization program and constant, intensive surveillance will continue to be necessary. The 1964 rubella disaster caused about 2,200 deaths, 1,800 cases of mental retardation and left about 12,000 children deaf or blind. I was alarmed, therefore, when I recently read that an outbreak of rubella, mainly among the young adult population in Los Angeles County, was reported by health officials. This disease can have devastating effects on the unborn. It would be unconscionable for us to allow explosive epidemics, reminiscent of the past, to occur.

England showed a dramatic increase in the incidence of pertussis disease from 1977 through 1980. As public confidence in the pertussis vaccination seriously declined, the resulting epidemic saw 102,500 cases of the disease, resulting in 28 deaths.

In the United States, the incidence of new tuberculosis cases is rising for the first time in 20 years. According to health authorities, the new cases are largely confined to the influx of migrants from areas of the world where TB is endemic, including Mexico, the Caribbean, and Southeast Asia. Reports from San Francisco and Miami show that, as usual, the disease spreads most readily where conditions are crowded. Although there is no vaccine for tuberculosis, the disease can be cured by a number of drugs discovered since the early forties, but the treatment regimen is lengthy

and requires a real commitment. To locate those in contact with new cases and to prevent the infection of others requires tireless detective work and continuous alertness.

Aside from the issues of funding and public disinterest, the immunization program is now threatened on another front—the fear of adverse health effects resulting from immunization. To combat this fear and to achieve and maintain high immunization rates, full public communication and health education is essential. The general public has a right to be given information about vaccines—even in areas of scientific and medical uncertainty. We must present the issues to the public clearly and accurately. There must be candid disclosure of the risks as well as the benefits of the vaccines. If a vaccination is not recommended for particular classes of individuals, that fact should be stated, and those high risk individuals screened, if possible, to prevent administration of the vaccine to them. Parents should be fully informed and on the lookout for adverse reactions associated with the vaccine. Accurate and timely reporting and statistical gathering on adverse reactions is critical in order that a realistic picture of the problems associated with the use of a particular vaccine can be compiled. Risks from vaccines also warrant increased efforts to produce safer vaccines.

It would be tragic if efforts to eliminate or control communicable disease were to become hampered because the public's confidence was so eroded as to cause frightened segments of the population to oppose and reject vaccines. Neither can we afford revival of serious childhood epidemics because a complacent and apathetic public, with a diminishing memory, forgets the iron lung. Public policy dictates that safe and effective immunization programs be implemented and maintained. This requires a system of adequate financing, public awareness, and understanding of the importance of vaccines, and promotion and incorporation of preventive medicine into the general health care system. To prevent pain and suffering and health care costs, we must vigorously guard against inadequate immunization of our children.

Today we will hear about the immunization programs from all perspectives. I am pleased to have with us officials from the Centers for Disease Control and the Food and Drug Administration. We will also hear from parents, legal counsel, physicians, and State health officials.

I am confident that the record we will develop will promote and protect our most valuable resource, our children.

I would like to welcome our first panel of witnesses, seated before us this morning: Dr. William Foege, Director of the Centers for Disease Control in Atlanta, Georgia; Dr. Alan Hinman, Director of the Immunization Division for the Centers; Dr. Harry Meyer, Director of the Bureau of Biologics and Director-designate of the Bureau of Drugs, Food and Drug Administration.

We will first hear from Dr. Foege, who I believe has a brief statement to make. If you could limit your statement to 10 minutes, we would be very appreciative, Dr. Foege. I know it is a very serious subject, but we do have the full statement for the record. I understand you have a colleague with you today that you would like to introduce to us.

Dr. Foege.

**STATEMENT OF DR. WILLIAM H. FOEGE, DIRECTOR, CENTERS FOR DISEASE CONTROL, ATLANTA, GA., ACCOMPANIED BY DR. DAVID FRASER, ASSISTANT DIRECTOR FOR MEDICAL SCIENCE, CENTER FOR INFECTIOUS DISEASES, CENTERS FOR DISEASE CONTROL; DR. ALAN HINMAN, DIRECTOR, IMMUNIZATION DIVISION, CENTERS FOR DISEASE CONTROL, ATLANTA, GA.; AND DR. HARRY MEYER, DIRECTOR, BUREAU OF BIOLOGICS, AND DIRECTOR-DESIGNATE, BUREAU OF DRUGS, FOOD AND DRUG ADMINISTRATION, BETHESDA, MD.**

Dr. FOEGE. Thank you, Senator Hawkins.

Yes; I do have Dr. David Fraser, who is Assistant Director for Medical Science with our Center for Infectious Diseases at CDC. I will, with your permission, enter the statement and summarize two areas—what has happened with the childhood immunization program, and then to look at our views on the use of the pertussis vaccine.

The first summary is on the childhood immunization program. As you have already stated, there are seven diseases recommended for vaccination by the Public Health Service. A major effort was launched in 1977 because of the fact that there had been a reduction in immunity levels in this country. You were absolutely right—parents have forgotten about iron lungs and the closing of swimming pools, and that over a third of children were not immunized for polio in 1977.

The results since the launching of this aggressive program in 1977 have been remarkable. At that time, there were 20 million children inadequately vaccinated. At the present time, 95 to 96 percent of all children entering school have been vaccinated against measles, rubella, polio, diphtheria, pertussis, and tetanus. But of even more importance, the suffering of children has been reduced. We had record low levels for five of the seven diseases in 1981. You have already mentioned the excellent accomplishment in measles. Last year, there were only 3,032 cases of measles in this country, an all-time low. And I am happy to report that during the first 4 months of this year, we are over 50 percent below last year's figures. Indeed, last week, outside of an outbreak in California, there was only one case of measles in the entire country that was not imported from other countries. So we are making remarkable progress on measles. We estimate that 15,000 cases of mental retardation have been averted because of the measles vaccination program.

In 1936, we recorded 7,000 deaths because of measles in this country, while last year we expect there will be no more than 2 or 3 deaths when the final figures are in.

Diphtheria, the only other specific disease I will mention before getting to pertussis, is equally remarkable. In 1900, diphtheria was the third leading cause of years lost prematurely—that is, before age 65—in this country. In 1981, there were only four cases of diphtheria reported in the entire country.

The program has not only been effective, it has provided an ideal example of Federal, State, and local partnership, as well as partnership between Government and the private sector. We estimate that half of all the immunizations given in this country to children

are given in the private sector; half are given in the public sector. And, as you pointed out, the Federal Government is supporting this through grant programs to States.

While vaccines are safe and are effective, they are not entirely safe, and they are not entirely effective. There will be people immunized who do not get protection. There will be people immunized who have an adverse reaction because of the vaccine.

For vaccines that are distributed in the public sector and paid for by Federal funds, we now require that an important information form that lists risks and benefits be provided to all people seeking immunization, and we require a signature from the recipient or from the parent or guardian of the recipient. The form also includes information on where to report if the patient has to visit a hospital, clinic, or physician within 4 weeks of receiving the immunization. Since this was instituted in 1978, we have had over 5,000 reports of adverse reactions, but I have to point out that the system is designed to detect clusters of adverse effects, in order to find a particular lot of vaccine that might be unusual. It is not designed to provide exact information on all adverse reactions.

Next, I would like to summarize our feelings on pertussis and pertussis vaccine. First, a word about the disease. Pertussis is a very debilitating disease, and instead of being a disease of 3 or 4 days or 1 week, it is frequently a disease of 2, or even 2½ months with severe coughing. It is a highly infectious disease with secondary attack rates in households as high as 90 percent. Complications do occur because of the disease itself, and a recent British study indicates one death per 1,000 cases, and one case of brain damage for every 10,000 cases of pertussis.

In the United States, we have studied 1,279 cases since 1979 and have found 29 percent to be complicated by pneumonia, 5 percent of the pertussis cases were complicated by seizures, 1 percent by encephalopathy, and 4 out of 1,000 children with the disease have died. The complications have been lower in those who have received one or more doses of DTP vaccine.

The trends in pertussis are very significant. In 1934, we recorded in this country over one-quarter of a million cases of pertussis with over 7,000 deaths. We currently average 1,000 to 3,000 cases reported per year and 5 to 20 deaths reported a year because of pertussis disease. We believe pertussis disease is underreported, and indeed in the last decade, the hospital discharge survey indicates about 3,600 hospitalizations each year as a result of pertussis.

Next, to look at vaccine effectiveness, recent studies in Great Britain during the epidemic that you mentioned have shown the vaccine to be between 70 and 90 percent effective. Recent studies in the United States have shown the vaccine to be 63 to 94 percent effective. And although there was a decrease in pertussis in this country even before vaccine was available, Dr. Mortimer of the American Academy of Pediatrics concludes that pertussis vaccine was the major reason for the decline in pertussis mortality in this country. His studies indicate that, without vaccine, we would experience as many as 1,000 deaths per year from pertussis in the 1970's. The vaccine effectiveness is underscored in both Japan and England, where outbreaks in pertussis followed a decrease in vaccination levels. I think it is important to note that the British Joint

Committee on Vaccination and Immunization concludes its report on the whooping cough epidemic of 1977 to 1979 as follows: "The decline in vaccine acceptance has led to a situation in which thousands of children have been subjected to a distressing and debilitating illness. Thirty-six have died, and an unknown number will have suffered from continuing ill effects."

Vaccine safety is an issue that we are very concerned about. Pertussis vaccine frequently causes local reactions, but in addition, a prospective study at UCLA on over 15,000 doses of OTP showed nine children with convulsions and nine with episodes of collapse, for a frequency of 1 in 1,750 immunizations for each complication. They had no cases of encephalopathy in that particular study. A large Swedish study of over 500,000 children showed one case of permanent brain damage for every 172,000 children immunized. In Scotland, a study showed brain damage in 1 out of every 135,000 children receiving three doses. And the British National Childhood Encephalopathy Study has shown permanent brain damage in 1 out of 100,000 children receiving three doses of vaccine.

We have to contrast this, of course, with brain damage in about 1 child out of every 10,000 who gets the disease.

We have also been concerned about the possibility of sudden infant deaths following vaccination because such deaths tend to occur during the same age as children receive vaccines, and there is therefore often a temporal association. The National Institute of Child Health and Human Development has done a multicenter study on sudden infant death. They have shown that there is no increased frequency of DTP immunization in children dying of sudden infant death as compared to matched controls. I think this is a very important study, because it alleviates some of the concern that we have had on Sudden Infant Death.

With DTP, we also require a standardized information form if the person is receiving DTP purchased by Federal funds. Only a small amount of DTP vaccine is actually purchased by Federal funds. Nonetheless, the forms have been widely distributed to the States, and most States use the forms even if the vaccine has not been purchased by Federal funds.

We have two major groups advising on safety and efficacy of vaccines in this country—the Red Book Committee of the American Academy of Pediatrics, which provides recommendations to pediatricians, and the Advisory Committee on Immunization Practices, which provides recommendations on public health practice. They continuously look at benefits and risks for vaccines, and indeed, a decade ago, this group, looking at the benefits and risks of smallpox vaccine recommended that smallpox vaccine not be given routinely to children any longer in this country, the point being that they sometimes take vaccines off their recommended list as well as adding vaccines.

Finally, recently there has been a television program on pertussis vaccine that has received wide publicity. It is my feeling that this program provided an excellent portrayal of the human suffering and pain which result from pertussis vaccine. The human price is a disturbing one. It should be known, and this documentary did us a service in that regard. However, the documentary failed to clearly spell out the price of disease. It did not show mental retar-

dation caused by pertussis disease. It provided no feel for an outbreak of pertussis with children of a village whooping through the night. It provided no pictures of caskets of small children who are victims of a preventable disease. It did not draw distinctions between bad medical practice and vaccine risk. And it allowed one person to seemingly convey the opinions of British medical authorities.

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An intelligent person watching that program could not make an informed decision on using pertussis vaccine. If journalistic malpractice were a recognized entity, I think the program would qualify.

The burden to wisely balance the benefits and risks of vaccine and disease for the maximum protection of the largest number of our children is not a light burden. It is a burden shared by health workers, by Congress, and by parents. But it is surely a burden also shared by the news media.

We would be happy to answer questions, Senator.

[The prepared statement of Dr. Foege follows:]

STATEMENT

BY

DR. WILLIAM H. FOEGE

DIRECTOR

CENTERS FOR DISEASE CONTROL

BEFORE THE

SUBCOMMITTEE ON INVESTIGATIONS AND GENERAL OVERSIGHT
COMMITTEE ON LABOR AND HUMAN RESOURCES

UNITED STATES SENATE

WASHINGTON, D.C.

MAY 7, 1982

I am pleased to be here to discuss with you the progress that has been made in conquering certain infectious diseases of childhood through vaccination. I will also summarize information about pertussis (whooping cough) vaccine, about which there have been many recent questions.

Modern vaccines are safe and effective. However, they are neither perfectly safe nor perfectly effective. This means that some individuals who receive vaccines will not get the desired effect--protection--and some individuals who receive vaccine will have an undesirable effect--a reaction. In developing vaccines, the goal always is to get a vaccine with the highest possible effectiveness and the lowest possible rate of side effects. In developing recommendations for the use of vaccines, there is a continuing balancing of the risks of disease, and the benefits and risks of vaccination.

In this country there are two main bodies which develop recommendations for vaccine use: The Committee on Infectious Diseases of the American Academy of Pediatrics (the "Red Book" Committee) and the Public Health Service's Immunization Practices Advisory Committee (the ACIP). The recommendations of the Red Book Committee are directed primarily at the private practitioner whereas those of the ACIP are directed toward the public health setting. The two groups maintain liaison with each other in order to ensure that the recommendations are consonant. Additionally, the Centers for Disease Control, the Food and Drug Administration, and the National Institutes of Health are represented at meetings of the two committees. Each of the committees meets 2-4 times a year to review recommendations on a scheduled basis and also to review new information which might affect current recommendations.

At present, there are seven diseases against which the Public Health Service recommends routine immunization of all children in the United States: diphtheria, measles, mumps, pertussis, poliomyelitis, rubella, and tetanus. Immunization normally begins at approximately 2 months of age with the infant receiving an injection of combined diphtheria and tetanus toxoids and pertussis vaccine (DTP) and a dose of oral polio vaccine (OPV). Similar doses of DTP and OPV are given at 4 months and a third dose of DTP at 6 months of age. At 15 months of age, the child receives an injection of measles, mumps, and rubella vaccine (usually in combined form as MMR), and then at 18 months of age the child receives a fourth dose of DTP vaccine and a third dose of OPV.

This completes the primary immunization series. Just before entry to school (at age 4-6 years) the child receives a further dose of DTP and OPV to ensure protection during the early years of school when transmission of communicable diseases is common. Throughout life, individuals should receive booster doses of tetanus and diphtheria toxoids approximately every 10 years to ensure that protection is maintained. The immunization schedule currently used in the United States is summarized in Table 1.

Children in the United States may receive their immunizations in a variety of different locations but most receive their immunizations either in the office of a private physician or in a health department clinic. Although there is considerable variation in different parts of the country, CDC estimates that, nationwide, approximately one-half of the children receive their immunizations in the private sector and one-half in the public sector, primarily in local health department clinics. Since 1963, the Federal Government has provided

support for public sector immunization programs through a categorical grant program, which is funded at $21.8 million for FY 1982. These funds help the states purchase vaccine for use in public programs as well as provide staff who are involved in educational and promotional activities, surveillance and investigation, and program management.

The widespread use of vaccines in the United States has had a remarkable impact on the incidence of these seven preventable childhood diseases and on the number of deaths attributable to them. Table 2 depicts the maximum number of cases and deaths of these diseases ever reported in the United States in a single year and compares these figures with the provisional total number of cases reported in 1981 and deaths reported in 1978 (the most recent year available). In 1981 record low levels were seen for five of the seven vaccine preventable diseases: Measles, mumps, polio, rubella, and tetanus. There were only four cases of diphtheria reported but this was one more than in 1980. The reported level of pertussis was lower than in 1980 but still was not as low as the total reported in 1978. These low levels of disease incidence are a result of the high levels of immunization in the nation's children. In the fall of 1980, 96 percent of children entering school for the first time had been protected against DTP, measles, and rubella; 95 percent against polio; and 92 percent against mumps. We do not yet have final figures from students entering school in the fall of 1981 but provisional results indicate that the levels will be essentially the same.

VACCINE DEVELOPMENT AND MONITORING

In the process of development, each vaccine undergoes testing in laboratory animals and then in a limited number of human volunteers before it is used on a wider basis in field trials. Immunity in both animals and man is determined in two different ways. The first of these depends on the fact that, with most diseases, the presence of antibodies in the blood correlates with protection. Consequently, one means of determining efficacy of vaccines is to measure the ability of the vaccine to induce formation of antibodies. The second means for determining the efficacy of vaccines is to observe their ability to protect the vaccinated individual against disease following exposure. For example, we commonly measure the protective effect of the vaccine when investigating outbreaks in school settings. Additionally, one can measure the effectiveness of the vaccine in preventing spread of disease from one member of a household to other members of the household who are or are not vaccinated. These types of studies go on both before and after licensure of the vaccine.

The safety of the vaccine is also studied both in animals and in humans prior to licensure. These studies typically involve relatively limited numbers of individuals and thus might not detect rare side effects of the vaccine. Following licensure of the vaccine, there may be very extensive use in the population and this initial experience may indicate the presence of undesirable side affects which might affect further use of the vaccine.

In the public sector, since mid 1978 the Centers for Disease Control has had a system for monitoring adverse events following immunization. The system works in the following manner: For each dose of Federally supplied vaccine

administered in the public sector an Important Information Form is used. This form summarizes the benefits and risks of vaccination and includes instructions that if the person who receives the vaccine has to visit a hospital, clinic, or physician in the 4 weeks following vaccination, that event should be reported to the health department. Information received by the health departments is then summarized and forwarded to the Centers for Disease Control. From the inception of the system in 1978 through the end of 1981 a total of 5,165 reports of adverse events following immunization was reported in this system. The system is designed to provide information about unusual clustering of known adverse events which might be associated with a particular lot of vaccine and to call attention to previously unrecognized serious adverse events following vaccination.

The monitoring system is not designed to provide exact information about the rates of adverse events following vaccination. It does not involve systematic follow-up of all vaccine recipients to inquire whether they have had an adverse event, and it affects only vaccines administered in the public sector, which account for approximately one-half of all vaccines. Despite these limitations, the system provides useful information and it would be difficult to provide major expansion or improvement of the system at any reasonable cost.

In the private sector, if practitioners see an untoward event which they feel may be related to vaccine they may report that fact either to the manufacturer, the Food and Drug Administration, or the Centers for Disease Control, or they may submit it as a case report for publication in the medical

literature. Additionally, there may be planned studies to look at the occurrence of adverse events associated with vaccination. One example of this type of study is the one carried out by Drs. Cody, Baraff, and Cherry at the University of California (Los Angeles) regarding reactions associated with DTP vaccination which will be discussed later.[1]

PERTUSSIS (WHOOPING COUGH)

I would now like to speak about pertussis and the vaccine that protects against it. A whooping cough-like illness can be caused by a number of different infectious agents, including both bacteria and viruses. However, most cases of this illness are caused by the bacterium Bordetella pertussis and this is the condition against which we vaccinate children. The illness caused by this organism is typically a protracted one with an initial period of non-specific respiratory symptoms lasting 1-2 weeks progressing to a stage of paroxysmal cough associated with a whoop on inspiration. The paroxysmal stage usually lasts 4-6 weeks but may last as long as 10 weeks. The disease is highly infectious and spread to susceptible family members is very common, with secondary attack rates in families as high as 90 percent. Complications of pertussis include pneumonia, otitis media, chronic damage to the lungs, convulsions, hypoglycemia, and brain damage. It is difficult to estimate with certainty the frequency of these complications. However, in recent studies in Great Britain approximately 4-10 percent of cases have been hospitalized; 4-18 percent of those hospitalized had pneumonia and 1.6-4 percent had convulsions.[2,3] Brain damage probably occurs in one of every 10,000 cases of

pertussis. Death occurs in approximately one in every 1,000 cases although the ratio of deaths recorded to numbers of cases reported varies in different countries, primarily as a result of differences in reporting practices.

Pertussis used to be an extremely common illness in the United States. As shown in Table 2, a maximum of more than 260,000 cases was reported in one year (1934). In that same year more than 7,000 deaths were recorded as due to pertussis. The incidence of pertussis in this country began to decline before the introduction of pertussis vaccine in the 1940s but the rate of decline has been greater since the vaccine was introduced (Figure 1). According to CDC's surveillance system, we currently average between 1,000 and 3,000 reported cases of pertussis each year and 5-20 deaths each year due to pertussis.

Despite the decline in the total number of cases reported per year since the 1940's, pertussis remains a serious problem in the United States. The Hospital Discharge Survey, carried out by the Public Health Service's National Center for Health Statistics, indicates that approximately 3,600 children were hospitalized for pertussis each year from 1970-1978, with an average length of hospitalization of 9 days.

In 1979, the Centers for Disease Control instituted a new Pertussis Surveillance System which obtains detailed information about cases of pertussis. Though hindered by underreporting of disease, the system has received reports on more than 1,000 cases from 42 States since its establishment in 1979. Although the system may preferentially receive reports of hospitalized cases, it is important to note that significant pertussis morbidity and mortality

continue. In 29 percent of children, pertussis was associated with pneumonia, in 5 percent with seizures, in 1 percent with encephalopathy (brain involvement), and in 4 cases per thousand, with death.

DTP VACCINE

Pertussis vaccine is a killed suspension of organisms or fractions of organisms with an aluminum absorbent. Current U.S. and WHO standards for the production and testing of pertussis vaccine represent the existing "state-of-the-art" but will undoubtedly undergo change in future years as additional data will be accumulated. However, pertussis vaccine has proved to be safe and effective in widespread use. Approximately 18-20 million doses of DTP vaccine are distributed annually in the United States, whereas less than one million doses of pediatric diphtheria and tetanus toxoids (which do not contain a pertussis component) are distributed, indicating the wide acceptance of the use of pertussis vaccine in this country. Pertussis vaccine is used almost exclusively with diphtheria and tetanus toxoids. All 50 States require immunization against a number of diseases prior to first entry into school and all require at least one component of DTP. Some state laws do not specify pertussis because the laws also apply to students at higher grades who would not normally be recommended to receive pertussis vaccine.

There were no generally recognized laboratory methods for determining the potency of the earlier pertussis vaccines. However, by 1948 a specific test

of potency involving a demonstration of vaccine-induced protection in laboratory animals had been developed. Standards for pertussis vaccine have been revised periodically since that date as the base of scientific knowledge relating to pertussis and pertussis vaccine has expanded.

Recent progress studying antigenic components of pertussis organisms suggests that two antigens (lymphocyte promoting factor, LPF, and fimbrial hemagglutination antigen, FHA) may be important inducers of protection. Both of these antigens can be prepared in a purified state and are being considered as possible new vaccines.

Problems in assessing the benefits of new vaccines include the fact that any new vaccine must induce equal or better clinical protection than the currently available vaccines and have an equal or lower rate of reaction. The low incidence of pertussis disease and the apparently good protection offered by current vaccines make clinical trials for efficacy very difficult in this country. Any trial large enough to measure differences in rates of serious or life-threatening reactions would be very expensive and difficult to carry out.

Since antibody production alone is not a consistent indicator of immunity to pertussis, vaccine efficacy is primarily determined by the protection conferred by vaccine in the face of exposure to disease. Recent studies of the effectiveness of currently available pertussis vaccines carried out in the United States have indicated a vaccine efficacy of 63-94 percent.[4,5] Studies carried out in Great Britain during the recent epidemic of pertussis

indicated vaccine efficacy in the range of 70-90 percent[6,7]. Recent evidence also indicates that persons who develop pertussis following vaccination have milder illnesses than those who have not been vaccinated.

RECENT EPIDEMICS FOLLOWING DECLINE IN PERTUSSIS VACCINATION

The effectiveness of pertussis vaccine has been questioned by some authors (particularly Gordon Stewart) who ascribe the decline in incidence rate of pertussis to general improvement in living conditions, etc[8]. In this country, Dr. E. A. Mortimer, formerly Chairman of the Red Book Committee of the American Academy of Pediatrics, made a detailed analysis of the incidence and mortality of pertussis and concluded that "It is unlikely that factors other than pertussis vaccine caused this decline in mortality."[9]

More dramatic evidence of the impact of pertussis vaccine and the seriousness of the illness itself comes from experience in Japan and England where declines in vaccination for pertussis vaccine were followed by major epidemics. The experience in Japan and England provides validation of the importance of routine pertussis immunization.

In Japan pertussis vaccination was put into practice on a nationwide basis in 1950. Before that time, the incidence rate of pertussis was greater than 100 cases per 100,000. By 1974, the incidence rate had decreased to 1 per 100,000. However, pertussis vaccine utilization in Japan decreased markedly in the last half of the 1970's after two deaths occurred following pertussis immunization. A major epidemic of pertussis followed with the incidence rate

of pertussis raising to to 11.5 per 100,000 in 1977 . The annual number of deaths increased from an average of less than 5 in the period 1970-1974 to an average of 32 during 1977-1979.[10] Thus, a decline in vaccination—prompted by two deaths possibly related to pertussis vaccine—led to an epidemic with more than 100 deaths.

Pertussis vaccine was first introduced into England in 1942. In 1957, pertussis vaccination became a national policy in England, although it was never mandatory. Between 1958 and 1974 an estimated 75 percent of children were fully vaccinated. Following allegations of adverse reactions after pertussis immunization, vaccinations declined and the estimated coverage of children fell to 30 percent by 1978. Pertussis case reports began to increase in 1977. A major epidemic occurred in Great Britain in 1978-79 with a total of more than 100,000 cases of pertussis and 36 pertussis deaths reported during this 2 year epidemic. The relatively low number of deaths in relation to the number of cases reported is thought to be due to improvements in the standards of living, nutrition, and the use of antibotics to control secondary complications. The British Joint Committee on Vaccination and Immunization concludes its report on "The Whooping Cough Epidemic 1977-1979" as follows: "...the decline in vaccine acceptance has led to a situation in which thousands of children have been subjected to a distressing and debilitating illness. 36 have died and an unknown number will have suffered from continuing ill effects."[2]

PERTUSSIS VACCINE: BENEFITS AND RISKS

There is widespread agreement that pertussis vaccine is effective in reducing the incidence of pertussis and the associated morbidity and mortality from the disease and its complications. In this country a study has been made of the costs, benefits and risks of pertussis vaccine.[11] The authors of that study state that "Without an immunization program, we predict that there would be a 71-fold increase in cases and an almost fourfold increase in deaths...per cohort of one million children."

In this study, which was based on the reported experience in Massachusetts, the authors estimated the likely number of pertussis cases and complications in a cohort of one million children, with and without a vaccination program. This analysis is shown below.

PREDICTED PERTUSSIS EXPERIENCE IN 1 MILLION CHILDREN

| | With Vaccination Program | Without Vaccination Program |
|---|---|---|
| Cases | 95 | 6,745 |
| Complications | | |
| Pneumonia | 5.9 | 152 |
| Seizures | 1.5 | 38 |
| Deaths | 0.3 | 7.6 |
| Encephalitis | 0.1 | 2.3 |
| Residual Damage | 0.03 | 0.8 |

As was mentioned earlier, no vaccine is perfect. Pertussis vaccine frequently causes temporary local and systemic reactions. The Food and Drug Administration recently supported a study at the University of California, Los Angeles.[1] In this prospective study of 15,752 doses of DTP vaccine and 784 doses of DT vaccine (without pertussis) the following reaction rates were found:

| Reaction | DTP Recipients | DT Recipients |
|---|---|---|
| Fretfulness | 53.4% | 22.6% |
| Pain | 50.9% | 9.9% |
| Fever | 46.5% | 9.3% |
| Local swelling | 40.7% | 7.6% |
| Local redness | 37.4% | 7.6% |
| Drowsiness | 31.5% | 14.9% |
| Anorexia | 20.9% | 7.0% |
| Vomiting | 6.2% | 2.6% |
| Persistent Crying | 3.1% | 0.7% |

Among those children receiving the 15,752 doses of DTP vaccine administered in this study, 9 had convulsions (7 associated with fever) and 9 had episodes of collapse, a frequency for each of these conditions of 1 per 1,750 immunizations. No cases of encephalopathy occurred in this study.

The major issue regarding reactions to pertussis vaccine is the possible relationship between the vaccine and encephalopathy with resulting permanent neurologic damage. Encephalopathy occurs in young children without any identifiable precipitating factor, and the fact that an event follows vaccination does not prove that it was caused by the vaccination. There is no distinctive clinical syndrome following pertussis vaccination. Encephalopathy following pertussis vaccination has been reported since the vaccine was first introduced. Several studies have estimated the frequency of encephalopathy following pertussis vaccination; almost all lacked a group of controls to ascertain the occurrence of encephalopathy unrelated to vaccination. Some of the major studies which have estimated rates of encephalopathy following pertussis vaccination are summarized below. In 1967, Strom published a summary of the experience in Sweden 1959-65.[12] He reported on 516,276

children who had received DTP vaccine in that period. 167 had some form of neurologic illness following vaccination (1 per 3,091 children vaccinated); 80 of these episodes represented convulsions, 54 shock, 24 abnormal screaming. Three children had permanent brain damage (1 per 172,000 children vaccinated).

In 1977, Gordon Stewart, one of the leading critics of pertussis immunization, reported on five children admitted to hospitals in Scotland between 1968 and 1972 with encephalopathy which began "soon after" receipt of DTP vaccine.[8] No attempt was made to rule out other possible diagnoses or other possible causes of encephalopathy. The study assumed that during that period 270,000 children had received 840,000 injections of DTP in Scotland giving an occurrence of encephalopathy of 1 in 54,000 children (1 in 168,000 DTP injections). Two of the children had permanent brain damage giving an estimated incidence rate of brain damage of 1 in 135,000 children (1 in 420,000 DTP injections).

The largest study of encephalopathy associated with DTP vaccination was the British National Childhood Encephalopathy Study, a case control study of 1,000 cases of encephalopathy admitted to hospitals in England.[13] Only 35 of the 1,000 encephalopathy cases had received pertussis vaccine within 7 days before becoming ill. By contrast, 34 of 1,955 controls matched for age, sex, and area of residence gave a history of pertussis vaccination within 7 days. Of the 35 cases, 32 had no history of previous neurological abnormality; at followup 1 year after acute illness, 21 of the 32 were normal, 2 had died, and 9 had evidence of developmental retardation. Using these observed figures and making certain assumptions about the vaccine coverage rate in the population,

the authors calculated an estimated risk of serious neurologic illness within 7 days of receipt of pertussis vaccine in normal children. This estimate is one instance in each 110,000 injections; the frequency of permanent damage present 1 year later would be 1 per 310,000 injections, approximately 1 in 100,000 children vaccinated. This figure should be contrasted with the estimated frequency of brain damage associated with pertussis infection (1:10,000 cases) and death due to pertussis (1:1,000 cases).

Death has been reported following pertussis vaccination, but these reports have been sporadic and do not fall into any consistent pattern. In 1978, four instances of sudden infant death syndrome (SIDS) were reported from Tennessee in children who had received DTP vaccine (from a single lot) within the preceding 24 hours.[14] A careful investigation of this episode was carried out including review of the vaccination history of all SIDS cases occurring in Tennessee during the 8-month period in which the suspect lot of vaccine was used and a comparable 8-month period in the preceding year. There was no significant difference in the proportion of children who died from SIDS who had received DTP vaccine within the preceding 24 hours in the study period compared with the comparison period.

Since mid-1978 the Centers for Disease Control has carried out a monitoring system for illnesses following immunization in the public sector. Table 3 summarizes adverse events reported following DTP vaccination from the inception of the system through 1981. Of the 44 deaths reported following DTP vaccination, 32 were reported as SIDS deaths. The other deaths had no consistent pattern and most of the infants had other conditions likely responsible for their deaths. Very few cases of encephalopathy were reported.

The National Institute of Child Health and Human Development has sponsored a multicenter case-control study of SIDS. Preliminary analysis of data from this study did not show any increased frequency of DTP vaccination among SIDS cases when compared to their matched controls. In fact, there was a lower frequency of DTP vaccination in SIDS cases than in controls.

The Red Book Committee of the Academy of Pediatrics and the Public Health Service's Immunization Practices Advisory Committee (ACIP) currently recommend routine administration of pertussis vaccine to infants beginning at approximately 2 months of age. A primary series of combined DTP vaccine consists of four 0.5cc doses given intramuscularly at (approximately) 2,4,6, and 15 months of age. At present 95 percent of children entering school have evidence of having received at least 3 doses of DTP (or DT) vaccine. Pertussis immunization is not recommended as a routine for children after the seventh birthday since pertussis is a very mild disease in older age groups and there is some indication that local reactions are more common in older children. It is important to note that a minimum of two doses (and probably three doses) is needed to induce protection at the 70-90 percent level. Therefore, young infants, the group at highest risk of death due to pertussis, are unprotected for at least the first 4 months of life. Their protection during this period derives largely from immunization of their older siblings who then do not transmit illness to them.

The medical profession is informed of the recommendations of the Red Book Committee through publication of the Red Book, circulation in Pediatric News and Comment, and publication of the recommendations in pediatric journals. The recommendations of the ACIP initially are published in Morbidity and Mortality Weekly Report which, with its circulation of over 100,000, reaches most public health professionals as well as the broadcast media, wire services, major newspapers, and news magazines. Articles relating to vaccine recommendations are published in many medical journals and medical news letters. The current recommendations of the ACIP on pertussis vaccine will be submitted for the record. The Red Book is in the process of revision; a pre-print of its new recommendations will also be submitted. This latest revision contains no major changes in approach from the previous recommendations.

The parents of candidates for pertussis vaccination learn about the benefits and risks of vaccination in a variety of ways depending on where vaccine is received. There is no standard method of informing patients in the private sector. In the public sector, a standardized system of Important Information Forms has been developed for use with federally supplied vaccine. These forms spell out in some detail the risks as well as the benefits of vaccination. Use of the forms is required whenever the vaccine is federally purchased. Since we do not have consolidated federal contracts for the purchase of DTP vaccines, only a small amount of DTP vaccine is actually purchased with federal funds and therefore subject to mandatory use of the Important Information Forms. The forms have been made available to States and they have been encouraged to use them even though the vaccine is purchased with State or local funds. Most States are using the forms. The current Important Information Form will also be submitted for the record.

RECENT PUBLICITY ABOUT PERTUSSIS VACCINATION

There is widespread agreement in the scientific community that the benefits of pertussis vaccination far outweigh the risk associated with the vaccine. Recently, however, a local TV station in Washington has produced and aired a 1 hour program on pertussis vaccine with the provocative and misleading title, "DPT: Vaccine Roulette." Although the program purported to present a balanced view of issues of safety and efficacy of pertussis vaccine, we consider that it presented a distorted view of the situation, focusing excessively on reactions known, suspected, or alleged to be due to pertussis vaccine, and giving very little emphasis to benefits of vaccination and risks of pertussis disease. There were many inaccuracies in the program. We are preparing comments on some of the inaccuracies in the script of the program and I would appreciate your permission to submit these comments for the record as soon as they are completed.

We consider the program to have been distorted, verging on the irresponsible. Unfortunately, it has been heavily promoted by the local TV station and it appears that attempts are being made to provoke a major controversy where one does not currently exist.

It is tragic that events such as brain damage may occur as a result of pertussis vaccination. However, we must all remember that pertussis itself causes complications more severe than these, and may cause death. Obviously, we all hope that improved pertussis vaccines will soon become available to make these rare untoward occurrences even rarer.

In summary, widespread use of vaccines in childhood has had a major impact on the occurrence of disease in this county. Continued use of vaccines is necessary in order to maintain the excellent progress that has been made to date.

This concludes my prepared testimony. I would be happy to try to answer any questions you may have.

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TABLE 1

## RECOMMENDED IMMUNIZATION SCHEDULE FOR CHILDREN

| *At this age:* | *Your child should receive:* |
|---|---|
| 2 Months | DTP (First)<br>TOPV (First) |
| 4 Months | DTP (Second)<br>TOPV (Second) |
| 6 Months | DTP (Third) |
| 15 Months | Measles, Mumps, Rubella* |
| 18 Months | DTP (Fourth)<br>TOPV (Third) |
| At school entry (4 through 6 years) | DTP (Fifth)<br>TOPV (Fourth) |
| 14 through 16 years and every 10 years thereafter | Td |

DTP: Diphtheria and tetanus toxoids and pertussis vaccine adsorbed (5 doses recommended)

TOPV: Trivalent oral polio vaccine (live) (4 doses recommended; however some physicians may elect to give one additional dose of TOPV at 6 months of age)

Td: Tetanus and diphtheria toxoids adsorbed (adult)

*May be combined as a single injection vaccine (MMR).

HHS:PHS:CDC:CPS:IM 10/81

TABLE 2

COMPARISON OF MAXIMUM AND CURRENT MORBIDITY AND MORTALITY DUE TO VACCINE-PREVENTABLE DISEASES UNITED STATES

| DISEASE | MORBIDITY | | MORTALITY | |
|---|---|---|---|---|
| | Max. No. Cases (Yr) | 1981 Provisional | Max. No. Deaths (Yr) | 1978 |
| Diphtheria | 206,939 (1921) | 4 | 15,000+(1921) | 4 |
| Measles | 894,134 (1941) | 3,032 | 6,986 (1934) | 11 |
| Mumps* | 152,209 (1968) | 4,729 | 55 (1952) | 3 |
| Pertussis | 265,269 (1934) | 1,189 | 7,518 (1934) | 6 |
| Polio (Paralytic) | 21,269 (1952) | 6 | 3,145 (1952) | 1 |
| Rubella** | 57,686 (1969) | 2,060 | 53 (1964) | 10 |
| Tetanus*** | 601 (1948) | 60 | 1,253 (1933) | 32 |

*First reportable in 1968
**First reportable in 1966
***First reportable in 1947

TABLE 3

REPORTED ADVERSE EVENTS FOLLOWING DTP
(ALL EVENTS WITH ONSET WITHIN 30 DAYS PUBLIC PROVIDERS ONLY)

| | 1978 (115) | 1979 (374) | 1980 (474) | 1981 (394) |
|---|---|---|---|---|
| Local reactions | 59 | 152 | 227 | 190 |
| Fever only | 19 | 55 | 79 | 57 |
| Rash | 17 | 56 | 59 | 66 |
| Allergic Reactions | 14 | 34 | 39 | 24 |
| Anaphylactic Reactions | 3 | 5 | 3 | 0 |
| Arthritis/Arthralgia | 2 | 4 | 9 | 3 |
| Convulsions: Febrile | 9 | 46 | 44 | 41 |
| Convulsions: Nonfebrile | 0 | 15 | 10 | 4 |
| Encephalopathy | 2 | 3 | 0 | 1 |
| Paralysis: Non-GBS | 3 | 2 | 5 | 0 |
| Other Neurologic | 13 | 32 | 41 | 37 |
| SIDS | 3 | 17 | 8 | 4 |
| Deaths: All Causes | 3 | 22 | 14 | 5 |
| Total Reports* | 115 | 374 | 474 | 394 |

*Some reports have more than one of the listed events.

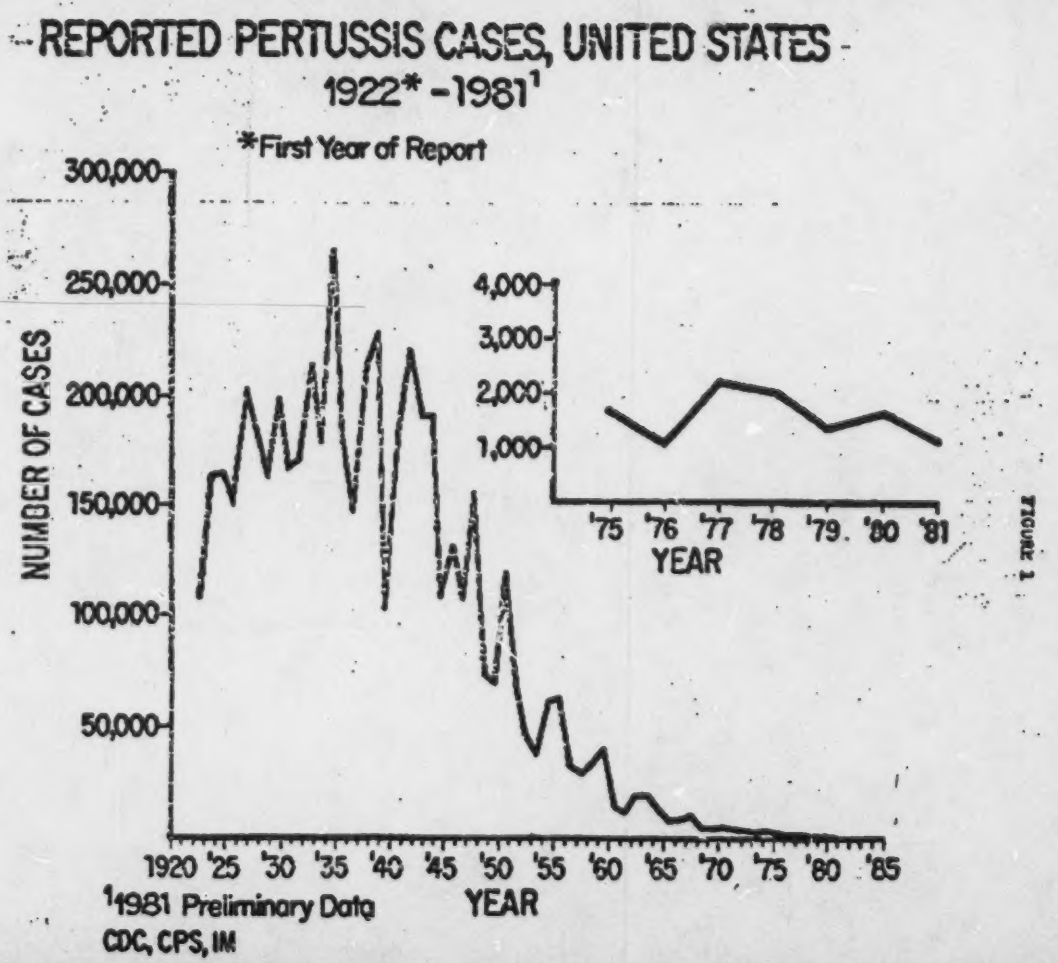
REPORTED PERTUSSIS CASES, UNITED STATES
1922* -1981[1]
*First Year of Report
NUMBER OF CASES
300,000
250,000
200,000
150,000
100,000
50,000
4,000
3,000
2,000
1,000
'75 '76 '77 '78 '79 '80 '81
YEAR
1920 '25 '30 '35 '40 '45 '50 '55 '60 '65 '70 '75 '80 '85
YEAR
[1]1981 Preliminary Data
CDC, CPS, IM

FIGURE 1

Senator HAWKINS. Thank you.

How do you respond to the statement of the American Academy of Pediatrics, that "if the President's proposed funding level of $28.8 million holds sway during fiscal 1983 for the childhood immunization program, vaccine delivery to children would be reduced to intolerably low levels?"

Dr. FOEGE. We are very sensitive, Senator Hawkins, to this problem. It is my feeling that because much of the backlog that I mentioned in 1977 has already been taken care of, and because we have a much more efficient immunization program than we had several years ago, that it should be possible to reduce costs. It has been our feeling that even though the costs have been reduced, we are hoping that some of the gaps will be made up by other funds. However, I want to emphasize that the Secretary has given me a very clear charge, and that is to monitor the immunization levels in this country, to keep track of how many immunizations are given, and to look at disease incidence. And the Secretary has said if we have slippage in these figures, that he immediately wants to have this reported to him, so that he can make corrections as needed.

Senator HAWKINS. CDC has said that budget proposals would cover the cost of immunizing only 3.8 million children, and perhaps as few as 3.4 million children, which is less than one-half of the number inoculated in 1981. Will this insure immunization of all children needing immunization?

Dr. FOEGE. It is true that the increased price of vaccine, which has been very substantial over the last several years, and the decrease in funds, will decrease the amount of vaccine that we can purchase. If this gap is not picked up by States by using the maternal child health grants or the prevention bloc grants, or by other ways, we will in fact relook at this to see what corrections have to be made.

Senator HAWKINS. I have seen statements that vaccine costs may go up as much as 30 percent this year. Have you seen like statements, or do you have any indication that the manufacturers are going to increase it by that amount?

Dr. FOEGE. Let me ask Dr. Hinman to give a statement on that.

Senator HAWKINS. All right—any of you that feel comfortable may answer.

Dr. FOEGE. Thank you.

Dr. HINMAN. The average price increase between 1981 and 1982 for vaccine that we purchased in the Federal sector was approximately 25 percent. It appears that there will be another further approximately 10-percent increase in the price of measles, mumps, and rubella vaccine for the remainder of this year.

Senator HAWKINS. Why? Do you know?

Dr. HINMAN. I think one would have to ask the manufacturer.

Senator HAWKINS. Well, as I understand it, 50 percent of the children are immunized by the Government; is that true?

Dr. HINMAN. Correct.

Senator HAWKINS. It seems to me that the Government should have a handle on the cost of that vaccine, if 50 percent of the total amount manufactured is purchased by the Government. Do the different manufacturers bid for this?

Dr. HINMAN. It is set out on a contract, with bids solicited. As it happens, there is a single manufacturer for measles, mumps, and rubella vaccine, a single manufacturer for polio vaccine, and there are three manufacturers for DTP vaccines at the present time.

Senator HAWKINS. So there is a single source for two, and then three for the DTP?

Dr. HINMAN. That is correct.

Senator HAWKINS. Our next investigation should be into the pricing of vaccine.

Isn't it true there is a direct correlation between Federal funding and the success of immunization programs in the various States?

Dr. FOEGE. It is true that the immunization levels in this country have improved markedly with the Federal program that was initiated in 1977. Many parts of the program have improved since then. We believe that there are more immunizations being given by a variety of people, but it is true that immunization levels did rise with the influx of Federal money in 1977.

Senator HAWKINS. Who would be the variety of people that give these vaccines?

Dr. FOEGE. Well, I think we have a program now that is so intermeshed with the health authorities, the education authorities in each State, voluntary agencies and parents who are involved, and the private sector, that I believe this is one of the best examples we have of a public health program that has incorporated nongovernment, private people into the program.

Senator HAWKINS. Advocates of a strong immunization program are concerned about the hard core of low-income children who do not receive immunization. I know that it is difficult to reach these children and that they are expensive to reach because they require tracking down by school nurses and public health authorities. How do you think the States will be able to maintain immunization levels and also reach the hard core of unimmunized children?

Dr. FOEGE. We have several programs that I will ask Dr. Hinman to describe on actually looking for the hard-to-reach through birth records and through hospital records.

Dr. HINMAN. Some of the activities, Senator, involve first of all, education programs in hospitals for new mothers at the time they are in the hospital to deliver their children. Before they go home, they are given information about immunizations, the necessity for immunizations, and an appointment for a first visit to the infant, which will not be an immunization visit. These programs are now in effect in, I believe, 35 States. Additionally, in the public health sector, a system of recalling children who miss appointments for needed vaccinations has been developed and is being implemented. We know that better than 95 percent of children in this country receive at least one dose of vaccine before their third birthday, so that——

Senator HAWKINS. Ninety-five, did you say?

Dr. HINMAN. At least one dose. They enter the system, and one of our problems has been trying to keep them in the system. And these recall systems, we hope, will be able to do that.

Senator HAWKINS. Has the Center for Disease Control made any recommendations with respect to problems associated with liability for injury resulting from immunization? You are notifying the

mothers as they have the babies that they should have these shots. Are they also told, or do you leave that responsibility to the doctor or the center that gives the shot, that there may be some side effects and what to do, if there are any? Whose responsibility is that?

Dr. HINMAN. Our important information forms, as Dr. Foege pointed out, mention risks as well as benefits of vaccination. They do not contain any information about remedies—legal remedies or compensation remedies—should an untoward event occur.

Senator Hawkins. Do they state what to do if there is an adverse reaction?

Dr. HINMAN. No; they say that one should contact the health department.

Senator HAWKINS. Has there been a recommendation with regard to compensation?

Dr. HINMAN. Not in the important information form.

Senator HAWKINS. It is my understanding that the CDC obtains information on total public immunizations from voluntary reports of States and local health departments. How accurately do you feel these reflect actual immunizations?

Dr. Hinman?

Dr. HINMAN. I think these reports are quite accurate in terms of doses of vaccine administered. A very high proportion of the vaccines—measles, mumps, rubella, and polio vaccines—administered in the public sector are purchased with Federal funds, and a part of the accounting system of the grant mechanism is to report vaccine administration. So we feel that figures for vaccine administered in the public sector are quite good.

Senator HAWKINS. Does the CDC compare the number of reactions obtained from its various sources to the number of vaccine doses distributed to determine adverse reaction statistics?

Dr. HINMAN. As Dr. Foege pointed out, the monitoring system we have is not designed to give exact rates of adverse events, because we know that there is underreporting. It is designed to provide us with an indicator of clustering of events or of the occurrence of unusual and previously unrecognized events. We have made comparisons of the number of reactions reported to us, compared to the number of doses administered, but this clearly represents a minimal estimate of the occurrence of adverse events following immunization.

Senator HAWKINS. Dr. Foege?

Dr. FOEGE. If I might just say, Senator Hawkins, we think that a better way of looking at the adverse effects is to have a specific prospective study, as the UCLA one. What we are looking for is, could there be a bad lot of vaccine. For instance, we have recently found children who had abscesses following certain vaccine, and it turned out that this could be related to a certain lot of vaccine. So our adverse effect surveillance system is looking for that kind of problem.

Senator HAWKINS. There is no way to determine if the vaccine is bad before you inject the child?

Dr. HINMAN. The vaccine in this case was not, in fact, bad, according to all of our current standards. It had a somewhat higher content of aluminum than most vaccines do, clearly within the limits which are spelled out in regulations. The occurrence of ster-

ile abscesses—these were not infections, but sterile abscesses—with this lot of vaccine was approximately 1 in 1,000.

Senator HAWKINS. If reliable data are not available on the actual number of total vaccinations, doesn't this result in an understating of adverse reaction rates?

Dr. HINMAN. As I pointed out, Senator, the figures we have do represent a minimal estimate, if we compare the number of reports we receive to the number of doses administered, because there is incomplete reporting. The system is not designed to provide us that exact information, however.

Senator HAWKINS. Do you feel a minimal estimation is enough? Is that adequate?

Dr. Meyer?

Dr. MEYER. If I could make a comment just to supplement what Dr. Hinman has said, it is easy to focus that any one system is the only system one has. We have already made mention of the British study, and there was mention made of Swedish data. The use of vaccines is an international concern, and you find many countries, many scientists, many health groups, all collecting data, and there is a great deal of interchange of data. So when you see a group of vaccine scientists, sitting down and looking at the question of adverse effects of vaccine, they are taking bits of data that come from many types of sources, through many types of studies, and from that, you are coming out with an estimate of what reactions are. And I think what Dr. Hinman is trying to say is the type of system which he is working with is particularly good at giving one type of information, but it also does give other types of information. For example, if some totally unexpected type of effect occurred with great frequency, it might very well be picked up by that type of system, and one might then initiate a prospective study to get more details. So there is no one system. There are many systems to work at a difficult thing, and the problem is to use systems that are basically cost effective, because acquiring information is not a free process.

Senator HAWKINS. Again, is a minimal estimate enough to give us the information we need to protect these children, or should we have more?

Dr. HINMAN. I think one can always feel that more information is desirable, Senator. In the process of development of vaccines as they are developed and then licensed and initially used, there are, in fact, trials that go on to look for the occurrence of more frequent side effects. These trials typically involve hundreds or thousands of individuals, and might not detect events that occur at a frequency of 1 in 100,000 or 1 in 1 million. Our system, we hope, will alert us to the occurrence of these rare events and then allow the design of studies to look more carefully at the occurrence of them.

Senator HAWKINS. Does the CDC feel more information is desirable, or do you get all you want or need?

Dr. HINMAN. One never has all the information that one would like.

Senator HAWKINS. Do you have any plans to develop a more exact information system?

Dr. HINMAN. We consider that the system we have can be improved, Senator. I do not know that it will ever be a complete

system. The only way that I can think of in which one would have complete information would be a direct followup of all recipients of vaccine—a personal contact of all recipients after they have received the vaccine—and that would be an undertaking that I think would be so cumbersome and expensive that it would not be feasible.

Dr. MEYER. If I can make a comment, too, to supplement what Dr. Hinman says there, one thing that would alter people's thinking is if the assessment of risk of vaccination, as compared to risk of natural disease, were a close assessment—in other words, if that balance were pretty close, you would clearly be prepared to spend a lot more money in trying to better define the risk. I think that most scientists would feel that the degree of confidence you have is such that you are certain that the risk of vaccination is far less than the risk of the natural disease. For example, if you are trying to make comparisons by better evaluation of vaccine, you would need to similarly made detailed studies of disease. No one has done that much of a detailed survey of the natural disease pertussis, in terms of very detailed followups of every patient. So that would be a gigantic undertaking. Since that balance between benefit and risk is very widespread, that causes persons again looking at the technology of today to feel that probably, where we are in 1982 is that the thrust of the best way to spend money at the moment is toward pushing for new generation vaccine. Our technology has progressed to the point where there is a very real chance that in the next decade, we can have vaccines that will be both more protective and also less reactive. Then, if one is going to spend more money evaluating, that would be the type of product to evaluate.

Senator HAWKINS. Is there any evidence to show that risk runs in families? I mean, if your father had a reaction to it, would your children be more apt to have it, and your children's children?

Dr. HINMAN. As far as the risk of paralysis associated with oral polio vaccine, there are certain types of inherited immuno-deficiencies which would make a child more likely to have a reaction.

In terms of other vaccines, I am not aware of data which would conclusively indicate that there is a familial risk.

Senator HAWKINS. On page 9 of your statement, it states, "When the pertussis vaccines were first introduced in this country, requirements for proof of safety and efficacy were not as stringent as they are today. However, the vaccine has proved to be safe and effective in widespread use and consequently, following a careful review of available information, it has been continued in the market." Have the pertussis vaccines been tested under current testing requirements for proof of safety and efficacy?

Dr. FOEGE. I would like to ask Dr. Meyer.

Senator HAWKINS. Dr. Meyer?

Dr. MEYER. You need to look at the documentation of biologics in terms of what I would call state of the art. You can pick almost any vaccine you wish, rabies vaccine or other vaccines, and what one approves at a particular time is based upon what is possible and feasible, again, looking at benefit and risk. The early pertussis vaccines would have been first approved in the early part of this century, at a time when the science base was much lower. The particular problem at that time would have been that you had demon-

strated clinically that it was possible to protect children with certain vaccines, but one had no good laboratory method of measuring the potency of those vaccines, and so there would have been great variation in potency from lot to lot. The big step forward, though, came in the 1940's, when it was possible for the first time to develop a potency test which involves the protection of experimental animals. Then through correlating those data with the English clinical trials that were done then, it was possible to demonstrate how many mouse protection units meant how much in terms of human protection. That test has been gradually refined since then, so that today, what you have in the United States, is the consistent pattern of being able to predict that the type vaccines you have on the market are uniformly protective—not 100 percent protective, but protective within the state of the art of those vaccines.

We are currently working, along with other international organizations, on new types of tests that we hope, in moving toward these vaccines of the future, will enable one to do even more precise controls. But this is the technology that is not quite yet with us.

Senator HAWKINS. The question was, have the pertussis vaccines been tested under current testing requirements for proof of safety and efficacy?

Dr. MEYER. The answer would be yes, Senator, because scientists would be confident—this would be broad scientific peer review of the data—would be confident that with the whole organism type pertussis vaccines which are being made internationally by current production technology, if those vaccines pass a certain number of units on the animal test which is done in the laboratory, protecting laboratory animals, it has been shown in clinical trials that that degree of protection will correlate with predictable protection in terms of clinical use. As Dr. Foege mentioned, this has been confirmed by surveillance of vaccine use in the past several years in this country, which has demonstrated that in fact those vaccines are protective.

But the simple answer to your question is yes, very definitely, yes.

Senator HAWKINS. In a March 8, 1982 report, Dr. Meyer, the GAO found that delays and missing reports hamper the FDA's adverse reaction system's ability to identify potentially serious reactions. Would you agree that the FDA needs all the information quickly if it is to make timely determinations on the need for regulatory action?

Dr. MEYER. Well, I think that report was dealing primarily with the Bureau of Drugs and not with vaccine reactions. However, the answer again would be yes, that we all agree we need the best information we can get. And one point I would make in reference to the system. You are not dealing with a static system. Just as there has been increase in vaccine standards in the state of origin and proof, there has been a considerable improvement over a period of years in surveillance systems. The systems Dr. Hinman mentioned did not exist a few years ago. The surveillance systems which we are using within the Food and Drug Administration, with which we interchange data with CDC, did not exist several years ago. We now have computerized all information that comes to us on adverse reactions. We exchange that information directly with CDC and

vice versa. If you went back even 5 or 6 years, you did not have that degree of standardization of the system. But I would say that 5 years from now, I think we will have even more refined systems than we have now.

Senator HAWKINS. Dr. Meyer, on page 5 of the written testimony, it states, "Once the vaccine is in use in the private sector, if practitioners see untoward events which they feel may be related to the vaccine, they may report this fact either to the manufacturer, to the Food and Drug Administration, or the Centers for Disease Control or they may submit it as a case report for publication in the medical literature." Do you actively solicit reports of adverse reactions from manufacturers?

Dr. MEYER. In terms of DTP vaccine—here again talking of surveillance systems—we receive from three manufacturers currently every report of every adverse reaction gotten to DTP. From two of the manufacturers, we receive it monthly, because they have it in their computer broken down that way, and from the third manufacturer, it is received quarterly, and that is reviewed by my scientists as it comes in.

Senator HAWKINS. Do you exchange reports of adverse reactions that you receive with the Center for Disease Control?

Dr. MEYER. Yes, we do. For example, Dr. Hinman mentioned the Sudden Infant Death Syndrome. We have all been interested in that. As we would receive data on that, we would notify CDC, they would notify us. And we have had many exchanges of information, and also, people from our shop visiting them and vice versa and trying to refine the system.

Senator HAWKINS. Do you determine, for instance, whether there is a duplication of adverse reaction reporting?

Dr. MEYER. Yes, insofar as you can from the data. It is possible that an adverse reaction could be reported through several systems—for example, USP might receive a notice of an adverse reaction. The same reaction might be reported to the manufacturer. At the same time, the same reaction might be reported to CDC. But if one can identify the source, one can usually determine that there is not duplication.

Senator HAWKINS. Is it possible that it could not be reported at all?

Dr. MEYER. Yes. As Dr. Hinman has said, adverse reaction reporting is always far less than complete.

Senator HAWKINS. Has the Department of Health and Human Services ever considered implementation of a mandatory reporting system for adverse reactions to immunization?

Dr. MEYER. I suppose I can speak for the Department of Health and Human Services generally. I know we and CDC and NIH have discussed many times over the years, in dealing with many vaccines, types of ways that we could obtain better data. I do not think we have reached the point of thinking that it would be cost effective to try to implement that type of system. As Dr. Hinman mentioned, the type of data that you would get from that type of system probably would not justify the degree of cost that would be involved in trying to get it.

Again I would stress what I said earlier. You need to remember that what I would call crude reporting of adverse reactions is only

one of many ways that you get a handle on what may be happening in terms of vaccine use. The most precise information usually comes from prospective or case control types of studies. This adverse reaction reporting is a general method, but it is not a perfect method. Even by spending a great deal more money, it would not be a perfect method.

Senator HAWKINS. Dr. Foege, in your written testimony, you state that brain damage probably occurs in 1 of every 10,000 cases of pertussis. In view of the flexibility of the reporting system, what is the source of the statistics?

Dr. FOEGE. I might ask Dr. Fraser, who has been looking at complications of both vaccine and pertussis, to comment on that.

Senator HAWKINS. Dr. Fraser?

Dr. FRASER. The answer illustrates again the use of different systems for gathering information. That estimate comes from a study in Great Britain, with their recent experience with their pertussis epidemic. But we also have some evidence from our surveillance of pertussis in this country, which suggests that the estimate of 1 in 10,000 may be a little conservative; that in fact, the risk from pertussis disease may be somewhat greater than that. But it is in that same range.

Senator HAWKINS. So the answer to my question is that it was a Great Britain study?

Dr. FRASER. The study that the 1 in 10,000 is based on is a Great Britain study. The study in the United States that more or less confirms it is based on our own surveillance.

Senator HAWKINS. On your own——

Dr. FRASER. Surveillance system, that is conducted by the State and territorial epidemiologists, in conjunction with the Centers for Disease Control.

Senator HAWKINS. For what year?

Dr. FRASER. For 1979 through 1981. That is an ongoing surveillance system. Our surveillance of pertussis was augmented in 1979 and has been continued at this augmented level since.

Senator HAWKINS. Dr. Fraser, I understand that you are an expert on pertussis. What would you tell parents who have become alarmed about adverse reactions to pertussis?

Dr. FRASER. I think pertussis is a very serious disease, and there is good reason to want to immunize against it. So I would be talking separately about the adverse reactions to the vaccine and the adverse reactions to the disease. I think the disease is especially severe in young children, and it is the reason why our vaccination program is targeted on young children.

The risk of having episodes where the children become breathless is 40 percent; the risk of——

Senator HAWKINS. Did you say "breathless"?

Dr. FRASER. Breathless. Just stopping breathing. That is 40 percent.

Senator HAWKINS. Forever?

Dr. FRASER. Not forever. Temporarily, fortunately. The risk of having seizures is 5 percent. The risk of developing pneumonia is 29 percent in the information we have. So that this is a disease we would very much like to avoid. The risk of death is about 4 in 1,000.

Senator HAWKINS. What symptoms or warning signals should parents look for?

Dr. FRASER. Well, the earliest symptoms of pertussis are not very specific. They involve a runny nose, a low-grade fever. The first clear symptoms of pertussis are when one gets into the paroxysmal phase, where one is coughing repeatedly, long sequences of coughing, in which the child gets progressively short of breath because of the difficulty in breathing, followed by a long whoop, as the child finally is able to suck air into the lungs.

Senator HAWKINS. Some of us remember that from having it in the home. I think younger parents may never have heard that.

Dr. FRASER. It is hard to forget.

Senator HAWKINS. What symptoms or warning signals should the parents look for from the adverse reaction from the vaccine, which I believe is the secret that has been held from them?

Dr. FRASER. Well, there are several reactions one can look for. One can almost expect a local reaction of swelling and tenderness and pain at the site of the injection. It is very common with the pertussis vaccine.

There is a risk of seizures, which occur about 1 in every 2,000 injections of the vaccine, and I think most parents can recognize a seizure when they see it.

There are children who develop persistent crying, where they just cannot be consoled, and this may occur in as many as 3 percent of children, who for several hours will cry and cry and cry, and that is very disturbing to parents and to the children alike. But it goes away after what seems like a long period of time.

And then there is the risk which, as Dr. Foege has mentioned before, of the encephalopathy, which is brain damage which can occur, it seems, at a very low risk of about 1 case in 100,000. And in that circumstance, the child may become lethargic, may show evidence of not being as alert as the child has been, and the child may not recover fully from that.

But in any of these evidences of severe reactions, it is well worth the parents contacting their physician or their health department, so that they can get further evaluation.

Senator HAWKINS. What do you think the high fever or the prolonged screaming indicates?

Dr. FRASER. The body has a reaction to the components of the vaccine. Many of those reactions are good and result in the development of antibodies that protect the child from subsequent exposure to the infection. However, with this vaccine, because it is not as benign a vaccine as we would like, sometimes that body's reaction is stronger than we would like, and that causes the swelling of the arms, the discomfort, and the crying may be as a result of the discomfort. Whether there are additional reasons for the crying is still something that is a topic——

Senator HAWKINS. Is there any evidence that it is a symptom of brain damage?

Dr. FRASER. There is not evidence that the large proportion of children who cry for several hours following the vaccine are brain damaged, no.

Senator HAWKINS. Do you have evidence of that?

Dr. FRASER. There has been examination, for instance, in the UCLA study, in the prospective study of screaming, of followup of the 3 percent of children who cried for several hours thereafter, and in all of those cases, the children recovered completely, and there was no evidence of brain damage.

Senator HAWKINS. Are there any plans to revise the information sheet that is given to individuals at public health centers with regard to DPT and what adverse reaction they may expect?

Dr. HINMAN. We periodically revise all of the important information forms. The current DTP form was last revised about 2 years ago and is probably about due for revision again.

Senator HAWKINS. I did not hear you. It is going to be updated?

Dr. HINMAN. It is probably about due for revision again.

Senator HAWKINS. What do private physicians do; do you have any knowledge of that?

Dr. HINMAN. They may do a variety of things. Perhaps Dr. Fulginiti can speak to this a little more later, when he testifies. But the Academy of Pediatrics is recommending that physicians discuss with their patients the risks and benefits of vaccination. They have also suggested that one way of insuring the transfer of information might be to use forms such as the important information forms we have developed, and the new edition of the Red Book, which is due out this month, I believe, will contain reproductions of the important information forms that we use.

Senator HAWKINS. In the UCLA study on the pertussis vaccine, I understand, the officials asked the parents to record their childrens' reactions that occurrred within 48 hours. Was that a sufficient period of time?

Dr. HINMAN. I think the majority of reactions that one sees with pertussis vaccine would be likely to become apparent within 48 hours. If one looks at the British childhood encephalopathy study, there was some difference in occurrence of encephalopathy in children who had received DTP vaccine between 48 hours and 7 days previously. The majority of the cases occurred within 48 hours of immunization, however.

Dr. MEYER. If I can make some comment about the UCLA study, there is some misconception as to what the intent of the UCLA study was, based on that TV program that came out. The UCLA study was actually designed to compare the acute period of reactivity to the several licensed vaccines that are currently used in this country from the standpoint of providing a current baseline with which to evaluate what we anticipate as new, improved types of vaccines, which we expect to have in use in the next several years. There was already a great deal of information from British studies and others, on general levels of reactivity, longer term reaction. What one was trying to generate in that study was, using the types of vaccines that are commercially available today, exactly how much reactivity does one see in the early period. As Dr. Hinman said, that is when most reactivity occurs, because then, if we have what I anticipate we will likely have, within the next year or so, one or more of these new types of vaccines to evaluate, we need something to compare it to. We have to see if that vaccine is in fact improved over what is commercially available. That was the intent of the UCLA study.

Senator HAWKINS. None of the children, in the UCLA pertussis study developed infantile spasms, and the report of the study states that this may be in part due to the brevity of the followup in this investigation. Why was there no followup done?

Dr. MEYER. Well, again, I would answer what I said a moment ago. The intent of the UCLA study was not to do a long-term evaluation of pertussis. There are many other types of studies which have provided some data on that. However, those children who had severe reactions were evaluated for longer than 48 hours. As Dr. Hinman says, at the time of the UCLA study, neurologists or pediatricians evaluated children with severe reactions for a longer period than just 48 hours, but there was no indication that the children were not normal at that time.

There is very little indication in the literature that I am aware of to indicate that a child who is normal throughout the first several weeks after vaccination then later develops something. I think most of the studies would suggest that adverse effects that are persistent, if they occur, will make their appearance early afterward, and that is true generally of reactions to many types of vaccines.

Senator HAWKINS. Are there any plans to complete this study?

Dr. MEYER. We consider that study, as I mentioned, Senator, more or less complete in providing us the data we want, which is the data to serve as the base for evaluating the new vaccines which we anticipate will be going to clinical trial in the next year or so in this country.

Senator. HAWKINS. But the new vaccine will not be available for some time, so we are still dealing with parents this year who have doubts in their minds as to whether to have these shots at this point in time.

Dr. MEYER. I would put that, again, in the context of my other comments, that one is looking at many other types of data. For example, there was a recent report. There has been a National Institutes of Health followup of children who had convulsive seizures after several types of vaccine, including DTP. That was a 7-year followup that we just reported this year, after 7 years. There have been other types of studies. So one is always dealing with a range of data that comes from many studies, and I would anticipate that before 7 years from now, I would like to think that we are going to have some of the new, improved pertussis vaccines. I will be very much surprised if we do not have some clinical trials of some of those vaccines within the next year or year and a half.

Senator HAWKINS. I will be, too.

Can you assure the American public today that thorough studies have been done on each of these vaccines, so that we know accurately the potential adverse reactions and can guard against them? That is directed to anyone who would like to respond. [Pause.] A clamour of silence there.

Dr. HINMAN.We would all be happy to respond to that. I think through the process of review of available information about vaccines, through the Public Health Service Advisory Committee on Immunization Practices, the vaccine review panels of the Bureau of Biologics, and the Committee on Infectious Diseases of the American Academy of Pediatrics, that we can feel comfortable that the

vaccines in use today are beneficial and that the benefits they confer outweigh any risks.

Senator HAWKINS. That is the statement for the panel.

Thank you so much. We will excuse you at this time.

Senator HAWKINS. Our next panel includes Mrs. Marge Grant, of Beaver Dam, Wis.; Mrs. Kathi Williams, representing Dissatisfied Parents Together; and Mr. Monty Preiser, who is an attorney with the law firm of Preiser & Wilson, in Charleston, W. Va.

We would like to begin with Mrs. Grant. We appreciate your participating in this hearing today and bringing to us the information you have and volunteering to discuss what has been a tragic and personal experience. All of us present today know that your testimony is essential, and we acknowledge and respect your willingness to come forward and help others, while sacrificing your privacy, and I thank you for addressing the subcommittee.

**STATEMENT OF MRS. MARGE GRANT, BEAVER DAM, WIS., MRS. KATHI WILLIAMS, ON BEHALF OF DISSATISFIED PARENTS TOGETHER, FAIRFAX, VA., AND MONTY PREISER, ESQ., PREISER & WILSON, CHARLESTON, W. VA.**

Mrs. GRANT. Thank you, Senator.

I wish to thank you for the invitation to appear as a witness before this committee. I have traveled here from Beaver Dam, as stated before, to share with you the devastation that was forced upon our family after our youngest son, Scott, received a type of DPT vaccine in the fall of 1961. From a bright-eyed, beautiful baby who had developed excellent head control and had progressed remarkably well, both physically and mentally, in the several weeks that followed those defective shots, Scott literally wilted before our eyes. His tiny body was thrown into near constant seizures that took his vision, and total head and body control. His eyes became crossed, and his head flopped around like a newborn infant. He lost his complete balance and sitting ability. He lost much of his sucking reflex and refused all solid foods. The real wonder is that he even lived. If he had, however, died at that time, I have no question he would have been diagnosed as a victim of SIDS, or sudden infant death syndrome, also called crib death, with cause "unknown." At least, this is what the so-called vaccine experts have been telling us.

Scott received a series of three shots of DPT plus polio at 4, 5, and 6 months of age, in the office of a prominent pediatrician in Madison, Wis. The doctor explained to me before he ordered his nurse to administer the shot that the type of DPT that Scott would receive was a quadruple vaccine because the polio component had been combined with the diphtheria, pertussis and tetanus. He told me the vaccine was called Quadrigen. He told me Scott may run a slight temperature for a short period, and he might be fussy. Unfortunately, never—and I repeat, never—once was I warned of any possible severe neurological injuries occurring from that shot.

And while he verbally explained the name of the vaccine to me, he did not record it onto Scott's medical records, which turned Scott's catastrophic injury into total chaos when we sued Parke Davis & Co., the manufacturer of Quadrigen.

Before I go into the grave injustice we have encountered through the entire court system, including the U.S. Supreme Court, I wish to reemphasize that Scottie did not display a fever after any of the shots.

Senator HAWKINS. At any point in time—he did not have a temperature.

Mrs. GRANT. He certainly did not, and this is really a frightening situation, but he never ran even a slight temperature.

Senator HAWKINS. How old was Scottie when he had his first DPT?

Mrs. GRANT. He was 4 months of age with the first shot.

Senator HAWKINS. And the next one?

Mrs. GRANT. And the second was at 5 months, and the third was at 6 months.

Senator HAWKINS. What symptoms did he have, other than loss of control of his head.

Mrs. GRANT. Right, well, those were the symptoms I explained earlier. I will be answering that in a second here.

Approximately 12 to 14 hours after the third shot, he gave forth an unusual, forceful outburst type of cry. That was the only cry. He acted frightened and as though he had a sensation of falling. I did not recognize at that time that this was indeed a signal of severe neurological problems, and I had not been told that I should look for anything like this, so I was not aware that this was a problem from the shots. Our doctor had not so much as hinted that this type of manifestation was a serious DPT reaction. This crying stopped upon my picking him up and holding him.

But between 2 to 3 weeks later—and I hope Dr. Foege and Dr. Hinman and Dr. Meyer will hear this—2 to 3 weeks later when I held him, I could only feel an occasional, tiny, unusual body movement. It was like a quiver. Again, at this time, I had no idea that this was a problem, or what these movements signified. I just thought he was a bit unsettled and possibly nervous. Those tiny jerks were not visible to the eye at this stage.

In the next several weeks, however, those occasional jerks progressively became more frequent, at which time the pediatrician ordered Scott to be hospitalized. After a total of 2 weeks of testing and evaluation, part of which were at the Mayo Clinic at Rochester, Minn., we were informed by the neurological experts there that Scottie had indeed suffered severe brain damage from the DPT shots. He was blind. He had suffered paralysis in all four limbs, and the tiny jerks that occurred several weeks earlier had become nearly constant, and were called myoclonic infantile seizures or spasms. This was at least 6 to 7 weeks later.

When we asked Dr. Gordon Millichap, the pediatric neurologist at Mayo what the potential was for Scott's recovery, he said in a very sad and somber voice that the future did not look good and that Scottie would probably be severely handicapped, both physically and mentally, for the rest of his life.

Dr. Millichap's diagnosis and prognosis could not have been more accurate, because despite the ardent efforts my husband, Jim, and I have put forth in literally combing this country to obtain effective treatment to rehabilitate Scottie's once whole and healthy body, today, at age 21, he remains an immobile, mentally retarded, spas-

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tic quadriplegic young man, and is dependent upon us for total, 24-hour-a-day care.

As I look back at this nightmare and the severity of Scott's injury, I do not believe he is just one unusual obscure case, who displayed almost no early symptoms, yet suffered profound permanent damage. I am convinced there is an extremely fine line, such as in Scott's instance, where major vaccine problems exist, but actually go undetected by parents until much later, when they are finally told the child's developmental deficits must be genetic. Can you image the trauma that must hit a parent? If they felt it was genetic, they would probably never have another child if this was their first child.

Now a word about our Government vaccine regulatory agency whose responsible duty it is to insure that only safe and effective vaccines are allowed onto the market, the Bureau of Biologics, which I shall refer to as BOB.

Judging from our personal experience with BOB, under the direction of Dr. Harry Meyer, in 1975, whom you saw here this morning, I must regrettably tell you that there is obviously much corruption involved between the vaccine manufacturers and this Governmental agency.

Senator HAWKINS. Why do you feel that way, Mrs. Grant?

Mrs. GRANT. Well, Senator, first of all, let me just state this. This governmental agency is supported by our tax dollars. We are the employer. They are the employee. We have hired those persons to protect us. And I just must tell you they are not doing their job. And I believe they should be dismissed from any responsibilities of this nature.

I will qualify this by relating our personal experience—and this dates back to 1974 and 1975, at which time BOB personnel totally obstructed our attorneys from obtaining crucial Quadrigen records, which were absolutely essential at that stage of trial preparation. Scott's attorneys made any number of requests prior to trial for the Bureau's testing records of Parke Davis' Quadrigen protocols, toxicity tests, adverse reaction reports, and others. The last request for those records was in a March 29, 1979, letter to Mr. Bozeman, Director of the Division of Compliance at the Food and Drug Administration. That letter was answered on April 9, 1975, by Edward Costello, Supervisor of the Public Records and Documents Center, in which he stated, and I quote: "The records you have requested will be furnished." See letter attached to my statement. Several weeks later on April 28, 1975, Mr. Ray Crossley—I wonder if he is in our audience; I would like to address this to him—he was the freedom of information officer, and he phoned our attorneys to tell them that the "adverse reaction" records along with others such as Quadrigen protocols going to the results of the Bureau's testing of various lots of Quadrigen were not being produced. Crossley said those records have "vanished". I would like to repeat that. Those records had vanished. The general meaning and Webster's Dictionary of the word, "vanished," means "to suddenly disappear."

This maneuver by BOB confirmed to us that those crucial records had been there, but Dr. Harry Meyer and his subordinates chose to make them unavailable. Those records were not lost or misplaced, as the Bureau told the Justice Department years after

the fact. And I predict BOB—and they have already talked this morning about their good recordkeeping and all these things—but I will predict they will attempt to convince you that yes, those records were lost, and they just cannot find them.

But now you know the truth of the matter, because Ray Crossley spilled the beans in that April 28 conversation, and you will see that letter attached to my statement.

Now in the same vein, I must tell you when Scott's attorneys subpenaed those same type of records from Parke Davis the attorney's name was William C. Roemer, and he was in charge of this type of information in the Parke Davis Detroit office. He said it was not possible to produce those records because they had been destroyed. Now, we are talking about the same records—the research records, the adverse reaction records and the testing of the various lots. Imagine. Parke Davis had destroyed its Quadrigen records of toxicity test results and those of adverse reaction. Think about the vanished records of BOB and the destroyed records at Parke Davis. Does this type of activity with crucial records sound coincidental to you, or is it an aspect of malfeasance?

What I have attempted to explain here is just a fraction of the obstruction to discovery that occurred at BOB and Parke Davis in our attempts to successfully prepare for Scott's trial. Time does not permit me to continue with more details, but if you will add to BOB's vanished records and to Parke Davis' destroyed records the fact that the doctor did not record the vaccine manufacturer's name and lot number onto Scott's medical records, you have the bottom line as to how the insurmountable obstruction prevented Scottie Grant from truly having his day in court. He lost his trial.

Please be assured, there was no question as to whether or not the DPT shots were the cause of Scott's injury. Five leading experts gave positive testimony at his trial that it was indeed the shots that crippled our precious son. As you are well aware, the so-called expert vaccine advisers tell us, "Oh, but the vaccine benefits far exceed the very few risks that occur." Those statements are not credible, because without an active and effective adverse reaction reporting system, they do not know how many kids they hurt, much less care.

I can tell you most assuredly, when it happens to your own child, there are no benefits; the risks are 100 percent.

I strongly urge you, Senator, for Scottie and the countless other vaccine victims that you will please do everything in your power to help rectify this vaccine nightmare. Remember, there are no special names on those vials of faulty vaccines—and the next victim really could be yours.

Senator HAWKINS. Thank you, Mrs. Grant, for your strong testimony. I understand that because of your experience, you were instrumental in changing the Wisconsin laws on immunization. What changes were enacted?

Mrs. GRANT. Yes; I was active, but there was a group that I worked with. I certainly cannot take the total credit. I did become very active in it, and the changes that were made were that instead of the State saying, "You must take them before entering school," we now have a personal conviction waiver that can be signed, and you can be exempt from them in Wisconsin. I also was

personally involved in convincing the legislators that every physician must record manufacturers' names and lot numbers, onto vaccine recipients' records.

Now, I do not really think, to be real honest with you, that that is enough in just one State. I believe that that should be a mandate at the Federal level.

[The prepared statement and additional material of Mrs. Grant follows:]

# T E S T I M O N Y

by

Mrs. Marge Grant

(mother of a DPT vaccine victim)

before

Chairman: Senator Paula Hawkins

Senate Subcommittee On Investigation In General Oversight

Labor and Human Resources Committee

Hearing held: May 7, 1982

Thank you for the invitation to appear as a witness before this subcommittee.

I have traveled here from Beaver Dam, Wisconsin, to share with you the devastation that was forced upon our family after our youngest son Scott, received a type of DPT vaccine in the fall of 1961. From a bright-eyed beautiful baby who had developed excellent head control and had progressed remarkably well, both physically and mentally --- in the several weeks that followed those defective shots, Scott literally wilted before our eyes. His tiny body was thrown into near constant seizures that took his vision, and total head and body control. His eyes became crossed and his head flopped around like a new born infant. He lost his complete balance and sitting ability. He lost much of his sucking reflex and refused all solid foods. The real wonder is --- that he even lived. If he had however died at that time, I have no question he would have been diagnosed as a victim of "SIDS" (Sudden Infant Death Syndrome). Also called, Crib Death, with the cause --- "unknown!" At least this is what the so-called vaccine experts have been telling us.

Scott received a series of 3 shots of DPT plus polio at four, five and six months of age, in the office of a prominent pediatrician in Madison, Wisconsin. The doctor explained to me before he ordered his nurse to administer the shot, that the type of DPT's Scott would receive was a quadruple vaccine because the polio component was combined with the diphtheria, pertussis and tetanus. He told me the vaccine was called, "Quadrigen." He told me Scott may run a slight temperature for a short period and he might be fussy. Unfortunately, never, and I repeat, never, once was I warned of any Possible severe neurological injuries occurring from the shot.

And while he verbally explained the name of the vaccine to me, he did NOT record it onto Scott's medical records. Which turned Scott's catastrophic injury into total chaos, when we sued Parke Davis and Co., the manufacturer of Quadrigen.

Before I go into the grave injustice we've encountered through the entire court system, including the U.S. Supreme Court, I wish to re-emphasize that Scottie did NOT display a "fever" after any of the shots.

Approximately 12 to 14 hours after the 3rd. shot, he gave forth an unusual and forceful outburst type of cry. He acted frightened and as though he had a sensation of falling. I did not recognize at that time that this was indeed a signal of severe neurological problems. Our doctor had NOT so much as hinted that this type of manifestation was a serious DPT reaction. This crying stopped upon my picking him up and holding him.

Between 2 and 3 weeks later, when I held him, I could "feel" an occasional tiny unusual body movement. Again, at this time I had no idea this was a problem or what those movements signified. I just thought he was a bit unsettled and nervous. Those tiny jerks were NOT visible to the eye at this stage. In the next several weeks however, those occasional jerks progressively became more frequent, at which time the pediatrician ordered Scott to be hospitalized. After about a total of 2 weeks of testing and evaluations, part of which were done at the Mayo Clinic at Rochester, Minnesota, we were informed by the neurological experts there, that Scottie had indeed suffered severe brain damage from the DPT shots; that he was blind; that he had severe paralysis in all four limbs; and that the tiny jerks that occurred several weeks earlier, had become nearly constant, and were called: "Myoclonic Infantile Seizures."

When we asked Dr. Gordon Millichap, the pediatric neurologist at Mayo's what the potential was for Scott's recovery, he said in a very sad and somber voice that the future did NOT look good --- and that Scottie would probably be severely handicapped both physically and mentally for the rest of his life.

Dr. Millichap's diagnosis, and prognosis, couldn't have been more accurate. Because, despite the ardent efforts my husband Jim and I have put forth, in literally combing this country to obtain effective treatment to rehabilitate Scottie's once whole and healthy body --- today, at near age 21, he remains an immobile, mentally retarded, spastic quadriplegic young man. And is dependent upon us for total --- 24 hour a day care.

As I look back at this nightmare --- and the severity of Scott's injury, I do not believe he is just one unusual obscure case, who displayed almost no early symptoms, yet suffered profound permanent damage. I'm convinced there is an extremely "fine line" such as in Scott's instance, where major vaccine problems exist, but actually go undetected by the parents until much later, when they are finally told the child's developmental deficits must be genetic.

NOW A WORD ABOUT OUR COVERNMENT VACCINE REGULATORY AGENCY WHOSE RESPONSIBLE DUTY IT IS TO INSURE THAT--- ONLY --- "SAFE AND EFFECTIVE" VACCINES ARE ALLOWED ONTO THE MARKET --- THE BUREAU OF BIOLOGICS --- WHICH I SHALL REFER TO AS: --- BOB ---

Judging from our personal experience with --- BOB --- under the direction of Dr. Harry Meyer, in 1975, I must regrettably tell you that there is obviously, much corruption, involved between the vaccine manufacturers and this governmental agency.

And since --- BOB --- is a governmental agency which is run by our tax dollars, please remember --- you and I are their employer --- they are the employees. We hired the persons at BOB to "protect us" --- I must tell you, I don't believe they are doing their job.

Please allow me to qualify, BOB personnel totally obstructed our attorneys, from obtaining crucial Quadrigen records, which were absolutely essential at that stage of trial preparation.

Scott's attorneys made any number of requests prior to trial, for the Bureau's testing records of Parke Davis' Quadrigen portocols, toxicity tests, adverse reaction reports and others. The last request for those records was in a March 29, 1975, letter to Marc Bozeman, Director, of the Division of Compliance, Food & Drug Administration. (FDA) That letter was answered on April 9, 1975, by Edward J. Costello, Supervisor, of the PUblic Records and Documents Center, in which he stated, and I quote: "The records you have requested will be furnished." Several weeks later, on April 28, 1975, Mr. Ray crossley, Freedom of Information Officer, phoned our attorneys to tell them that the "adverse reaction" records, along with others such as Quadrigen protocols going to the results of The Bureau's testing of various lots of Quadrigen, were NOT being produced. Crossley said those records have "VANISHED." Please allow me to repeat that. Those records had VANISHED!

The general meaning, and Webster's definition of the VANISH --- means to "suddenly disappear.

This maneuver by BOB, confirmed to us that those crucial records, had been there, but Dr. Harry Meyer and his subordinates chose to make them unavailable. Those records were NOT lost or

misplaced as the Bureau told the Justice Department --- years after the fact. And I predict BOB will attempt to convince you, of the same exucse. But, now you know the truth of the matter, because Ray Crossley spilled the beans, on April 28, 1975. (please see attached letter.)

Now in the same vein, I must tell you when Scott's attorneys subpoened those same type of records form Parke Davis' attorney, William C. Roemer, who was in charge of this type of information in Parke Davis' Detroit office, he said it was not possible to produce those records, because they ahd been "DESTROYED." Imagine, Parke Davis had destroyed its Quadrigen records of toxicity test results, and those of "adverse reactions." Think for a moment --- VANISHED records at BOB --- and DESTROYED records at Parke Davis. Does this type of activity with crucial records sound coincidental to you? What I've attempted to explain here is just a fraction of the obstruction to discovery that occurred at BOB and Parke Davis, in our attempts to successfully prepare for Scott's trial. Time does not permit me to continue with more details but if you will add to --- BOB's VANISHED records, and to Parke Davis' DESTROYED records, the fact that the doctor did not record the vaccine manufacturer's name and lot number onto Scott's medical records --- you have the bottom line as to how the insurmountable obstruction, prevented Scottie Grant from truly having his day in court. He lost his trial.

Please be assured, there was no question as to whether or not the DPT shots were the cause of Scott's injury. Five leading experts gave positive testimony at his trial, that it was indeed the shots that crippled our precious son.

As you are well aware, the so-called expert vaccine advisors tell us --- oh, but the vaccine benefits far exceed the very few risks that occur. Those statements are not credible, because without an active and effective adverse reaction reporting system, they don't know how many kids are being hurt --- much less care. I can tell you most assuredly, WHEN IT HAPPENS TO YOUR OWN CHILD, THERE ARE "NO BENEFITS" AND THE RISKS ARE 100 PERCENT!

I strongly urge you, for Scottie, and the countless other vaccine victims, that you will please do everything in your power to help rectify this vaccine nightmare. Remember, there are no special names on those vials of faulty vaccines --- the next victim --- could be your's.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

April 9, 1975

Mr. Arlo McKinnon
Kersten & McKinnon
231 West Wisconsin Avenue
Milwaukee, Wisconsin 53203

In reply refer to:
File No. F 75-1205

Dear Mr. McKinnon:

This is in reply to your letter of March 29, 1975.

[redacted]. There will be some delay in retrieving these documents, but you will hear from us as soon as the search is complete.

Sincerely yours,

Edward J. Costello
Supervisor
Public Records and Documents Center

KERSTEN & McKINNON
ATTORNEYS AT LAW
231 WEST WISCONSIN AVENUE
MILWAUKEE, WISCONSIN 53203
(414) 271-0054

ARLO McKINNON
E. CAMPION KERSTEN
GEORGE P. KERSTEN
KENAN J. KERSTEN
KEVIN M. O'DONNELL

CHARLES J. KERSTEN
(1925 - 1972)
J. P. McKINNON
(1943 - 1973)

April 28, 1975

Mr. Benjamin Gordon
Senate Small Business Committee Office
Russell Senate Office Building
Washington, D.C.

Dear Ben:

The enclosed copy of our letter to Ray Crossley (Freedom of Information Officer, Bureau of Biologics) indicates when we will next be in Washington to look over whatever documents the Bureau of Biologics has assembled for us. While at present we have tentative dates to examine these documents on Thursday May 15 and Friday, May 16, we are trying to advance this to Thursday, May 8 and Friday, May 9. We will notify you when the dates are firm so that we can arrange to see you also when we are there.

In his long distance talk with us today, Crossley stated that none of the Quadrigen protocols (testing reports, etc.) for the years prior to Parke Davis' so-called "by-pass" protocols on Quadrigen (after 1962) are available. In other words for the crucial years involved here, from about 1953 to 1962 inclusive, these important Quadrigen protocols going to the results of their testing of various lots of Quadrigen for decision as to whether they should be licensed or released to the market, are not being produced. [redacted]

Also the so-called adverse reactions or complaints files and correspondence, reports, etc. regarding Quadrigen are not being produced because as Crossley explains this, apparently such adverse reaction files, reports, complaints and correspondence were not kept in a central file by the Bureau of Biologics, formerly the Division of Biologic Standards of NIH under HEW. This is particularly hard to accept in view of the almost continuous history of major litigation and claims regarding the catastrophic adverse reactions of Quadrigen, commencing with the Stromsodt case in 1959, which adverse reaction reports and complaints were preceded by many reports of such adverse reactions during the clinical and other testing of Quadrigen before it was licensed in March 1959.

George Kersten and I should like to discuss all of this with you when we are in Washington on May 15 and 16. In the meantime, if there is anything you may do to assist in locating such adverse reactions files, correspondence and the Quadrigen protocols prior to the middle of 1962, all of which are missing or unavailable, it would certainly be helpful and appreciated.

In respect to complaints about Quadrigen, Crossley mentioned that some of these complaints and correspondence might be known to the Center for Disease Control (CDC) which apparently is a division of the U.S. Public Health Service, the latter in turn being under HEW. He mentioned the Director was Dr. David J. Sencer, area code 404, 633-3291. Perhaps a phone call or approach from you, Ben, to Dr. Sencer might develop some information as to where this adverse reaction material and complaints about Quadrigen are.

You may have occasion to mention to Senator Nelson that both Mr. and Mrs. Grant, the parents of the child, have repeatedly expressed their appreciation of the help he and you are giving us and them in which the future care and welfare of their quadraplegic child is at stake.

Sincerely,

Arlo McKinnon
for
KERSTEN & MC KINNON

tm

cc: Mr. and Mrs. James Grant

Enclosure

Mr. and Mrs. James L. Grant
602 S. University Ave.
Beaver Dam, Wisconsin 53916

January 2, 1977

President-Elect and Mrs. Jimmy Carter
Plains, Georgia 31780

Dear President and Mrs. Carter:

We are just delighted that you won the election! Rest assured, you got both of our votes and all we could muster up besides.

Our reason for writing you at this time, pertains to a subject in very serious need of attention because it is affecting, all Americans. "Harmful Drugs." In our immediate family it's been a personal catastrophe, to say the least. We bring this personal experience to you, with a most sincere hope you will help us. To dissertate its entirety would become voluminous, so we will try to give you as accurate a picture, as briefly, as possible.

We have felt ever since you folks came into the top title of our nation, it is our moral obligation to tell this tragic, true story to someone in authority, who is honest, if it is ever to be rectified. "Rectified" that is, as much as is possible at this late date, for our 15½ year old "Quadriplegic" son, Scott, who suffered irreversible, severe brain-damage in his early infancy, after receiving inoculations of a 4-in-1 product known as "Quadrigen."

On June 4, 1961 we were blessed with our second "much wanted" child, a son, completely healthy, who progressed "exceptionally well" from birth to 4 months of age. Less than 4 months later, we were informed by medical experts that he had suffered a severe brain-insult; that the prognosis for his future was very very poor; he would be mentally and physically retarded, and crippled the rest of his life! Naturally, this, in itself was beyond acceptance, but we loved him dearly and felt since we had been given a beautiful, normal child at birth, who had gained excellent head control and vision before 3 months of age, perhaps, it would return. So with many tears, perseverance, and faith that God would help us, we gave our absolute "all", physically, financially, and mentally to rehabilitate his once whole and healthy body. Despite our past 15½ years of diligent efforts, Scott remains a totally dependent child!

Scott received a series of three Quadrigen injections in fall of 1961, at four, five, and six months of age. These inoculations were intended to immunize him from Diphtheria, Tetanus, Pertussis (whooping cough) and Polio. All four components were combined and administered with one injection.

Quadrigen, through previous Court decisions was proven a "defective vaccine" as formulated, manufactured and distributed by Parke, Davis and Co., and because of Quadrigen's history of dangerous qualities and severe injuries to infants, numerous cases had been litigated, and won, at the time that we too, brought suit against Parke, Davis and Co. Detroit, Michigan.

Since the merger of Parke, Davis and Warner Lambert was allowed during the Nixon regime, it is an extraordinarily big drug Co. if not, "the biggest" in the United States.

During pre-trial preparations in April of 1975, our attorneys were in Washington in an attempt to locate information within the FDA, on research and marketing data, of Quadrigen. The enclosed copies of letters will document what happened after they contacted Senator Nelson's office, for assistance.

Just how, do important testing and marketing records VANISH?! We might add, "so conveniently" for Parke, Davis just a few weeks before going to trial. Not only did someone within FDA lose these records (for Parke, Davis) but when our attorneys went right to their office in Detroit, with a subpoena for ALL Quadrigen records, Parke, Davis' attorney there in charge, William C. Roemer, testified under oath that all pertinent records had been destroyed! His excuse was that it was simply done in the "normal course of business."

What we've attempted to explain here, is a mere fraction of the "obstruction" to discovery, produced by Parke, Davis, during our ardent efforts preparing for trial. However, since there was no way, we could properly prepare for trial with the above behavior, Federal Judge Reynolds, then applied what is legally called, "Collateral Estoppel." This means Parke, Davis was legally stopped from again trying to prove their product, Quadrigen, was safe. Judge Reynolds saw fit to take this action because in several previous trials this very vaccine had been "proven" defective, and why should victims have to prove over and over, what had already been well established.

Please keep in mind .... prior to, the judge's ruling of collateral estoppel, Parke, Davis in numerous sworn statements and in oral testimony had said they had "no records" to prove Scott's Pediatrician did, or did not, purchase Quadrigen in the relevant period (June through December of 1961). Please keep in mind also, Scott's Pediatrician testified in earlier depositions that he HAD infact purchased Quadrigen, but not always through a pharmacy, instead, by what he called drop, or bulk shipments. The difference was, this type of transaction was done "directly" with Parke, Davis .... but, he did not have "purchase records" of Quadrigen bought in this manner.

Ironically, after Parke, Davis had learned positively that Scott's doctor did not have purchase records of "bulk" shipments .... and, after Judge Reynolds' collateral estoppel ruling .... Low and behold! Parke, Davis suddenly "found" records .... and, (in an employee's desk drawer yet)! They claimed, these records proved no Quadrigen had been produced or shipped through the last half of 1961. What's more .... they also suddenly found "52 Cartons" more, of other marketing records in a Skokie Illinois branch office, which would have supplied Wisconsin doctors. Coincidentally though, the "Inventory Record" of the time in question, was no longer around!

We went to trial on June 2, 1975 with two weeks of presentation by Scott's witnesses. Every last one of his treating Physicians, including his "Mayo" Neurologist testified: Yes, it was the Quadrigen that brain-damaged and caused Scott's permanent paralysis.

Judge Reynolds then recessed for one week.

Then came the final week in which Parke, Davis presented its side of pure unadulterated deception. Their "objections" on cross examination were continuous, to the point the jurors were out of the Court room more than they were in! Unfortunately, Parke, Davis convinced Judge Reynolds throughout trial, that because collateral estoppel pertained to the "defect" in Quadrigen, to tell the jury anything of the "details" of the defective vaccine, should not be allowed, and it wasn't. Consequently, much evidence was suppressed by over-extending the collateral estoppel ruling. Instead of it working as a sword for Scott (which it should have done) it provided a shield, for Parke, Davis. And it allowed them to present a very very false picture to the jury! The Jury was led to believe all the records Parke, Davis presented were authentic, original, and complete. They were never told of the VANISHED FDA records, or of the destruction of files in Detroit, or of the missing inventory record, in the Skokie office.

Most important of all .... the jury was not told that outdated Quadrigen was never RECALLED from the shelves of Pharmacies, Physicians, etc. Nor was the jury told that the doctors throughout the country had never been informed, that as of April 1961, the Government had ordered a shorter shelf life, to be observed. For example, to give you perhaps a better picture: Before April of 1961, any Quadrigen made let's say in January of 1961, would have had stamped on the vial an expiration date of January 1962. Naturally, since the doctors were not told they shouldn't use any of that January 1961 vaccine, after June, of that year, they innocently continued to administer the toxic Quadrigen, that became more and more poisonous with each passing day!

Wasn't it kind, considerate, warm and humane, for both Parke, Davis and FDA .... to very casually and quietly allow all that poisonous Quadrigen out there in Physicians' offices to be injected left and right into innocent beautiful infants .... knowing full well, the vaccine could, and would, injure them for life!!

The trial itself ended on a Friday. Then Judge Reynolds recessed the jurors again, to go home over the weekend, before their deliberation on Monday. ( A full week recess, between presentations .... plus, a weekend at the finish, is a lot of time .... to forget!)

In deliberation, the one younger juror convinced the others, the records showed, there was simply no Quadrigen made or shipped through the relevant period, so, Scott Grant could not have received it. Four, of the six jurors held out for several hours, saying they felt Parke, Davis was guilty. But, this younger juror (a mother of 3 small children) emphatically informed the rest .... that if they sat there another whole week, she would NOT vote against Parke, Davis .... because they were innocent! Finally, all felt they had to agree with her, if they wanted to get the job done, before, July 4th! So, they gave in to her, and brought in a verdict against Scott.

A serious, unanswered question remains in our mind .... could there have been "tampering" with the youngest juror?!

After this bitterly fought trial and heartbreaking verdict, we finally garnered up enough courage, and money, to take the case to the U.S. Appellate Court in Chicago, feeling certain, this had to be a victory. It wasn't!! Despite the judges there, admitting previous errors had been made, they affirmed the original decision.

We will swear with our hand on the Bible .... that .... if, the verdict of the six woman jury: that Parke, Davis is innocent .... is just. And if, Judge Reynolds' endorsing their verdict was done in the best interest of justice .... And if, the three panel appellate judges' decision was given in sincere conscience, of absolute justice .... then we have witnessed the absolute ultimate, in "Mockery" of the U.S. Judicial System!! It's too bitter-a-pill.... we simply cannot swallow it!

It's totally evident to us, if the guilty can lie, deceive, and cheat enough to fit within a certain "legal rule" the sky's the limit!! Pray-tell, is that what our Constitution is all about? Or have our human-rights been twisted by legal jargon, to fit the criminal? which brings to mind: is the subject of Quadrigen .... Civil or Criminal? In its litigation it was treated as civil. Frankly, it's been our contention all along that the history of Quadrigen is criminal, rather than civil. After all, it killed and crippled human beings .... what's civil about that?! Parke, Davis and FDA both, were fully aware of Quadrigen's deleterious effects on infants, before, it was released onto the commercial market in 1959.

Another exact example, at this very point in time, of obvious corrupt binds between drug companies and top government officials, is the "Swine Flu Hoax." Again, "Parke, Davis" is right in there pitching .... gleaning a good share of the 135 million fiasco!

WHERE DO WE GO FROM HERE?? .... After already investing $35,000.00 of "borrowed" money for Scott's litigation, none of which went for attorney fees, we seriously question whether it's worthwhile taking it to the U.S. Supreme Court, since so few cases are accepted there. Yet, here's our precious helpless son laying and depending on us, to help him. We simply do not have a choice, and feel profoundly, if ever there was a case of Constitutional nature, or one of national concern, it's Scott's.

Health freedoms are inherently guaranteed to us as human beings. And our right to them as Americans is implied in the words, "Life, liberty and the pursuit of happiness." In Scott's life, these freedoms and rights have been denied him entirely, since the severe Quadrigen injury! The freedoms and rights have been denied him as a result of unopposed pressures from a huge organized pharmaceutical manufacturer, Parke, Davis and Co., working hand-in-glove with the nation's corrupt governmental agency, the FDA, whose laws and regulations have been imposed to better serve the drug companies, than the public at large.

Our attorneys will be filing Scott's case with the U.S. Supreme Court in Washington, D.C. by or before January 25, 1977.

We earnestly beg of you, President and Mrs. Carter, please, if there is any thing you can do, that Scott's case will be accepted etc., you will have made possible for him, the very first step, in the direction of justice.

Our attorneys are not aware of us writing this letter, and we have been motivated to do so, by our sheer desperation!

Our very best wishes and prayers, go with you to the White House.

Most Sincerely

Mr. and Mrs. James L. Grant

Enclosures

THE WHITE HOUSE

WASHINGTON

October 14, 1977

Dear Mr. and Mrs. Grant:

This is a follow-up to my letter of August 5. Your letter to the President concerning your son, Scott, has evoked the deepest sympathy and concern here at the White House.

Although you alone can fully comprehend the tragedy you and your son have suffered, your courageous forbearance in the face of this adversity is apparent and compels the admiration of any who perceive your situation. Despite his tragic affliction, Scott certainly is fortunate in having dedicated and unselfish parents such as yourselves.

In your letter to President and Mrs. Carter, and again in your correspondence with Mr. Judd Kutcher, Assistant General Counsel for the Administrative Office of the United States Courts, you have expressed alarm at certain aspects of the litigation in which your son was plaintiff and which was resolved in favor of the defendant.

At present both the Court of Appeals and the Supreme Court have concluded that Scott's appeal lacked merit on the basis of the record made in the District Court. I can offer you little encouragement in this regard other than to assure you that we have full confidence in the integrity of our Federal appellate courts.

It may allay your concern somewhat to know that the Supreme Court each term fully considers hundreds of petitions for certiorari. More often than not, those petitions which are denied are done so without comment, unless one of the reviewing justices dissents from the otherwise unanimous opinion of his colleagues that a particular appeal lacks merit. This does not mean that your case and the arguments you made on appeal were not fully considered by the Court. Be assured that they were so considered.

D

Also, it is my understanding that notifications from the Clerk of the Court of denials of certiorari are regularly sent in the form which you received. Although perhaps a necessary concession to the realities of the work load at the Supreme Court, it is understandable that such an abrupt, impersonal communication is unsettling to you in the circumstances.

I am confident that your lawyer can explain to you that the appellate courts are permitted to review only those facts which appear in the record of trial and questions of law which arise from such facts.

Thus, if new evidence were discovered in a given case or it was established that a party to a lawsuit illegally obstructed proceedings in order to obtain a favorable result, then a new trial might be in order even though a previous appeal was unsuccessful. Of course, such a development is rare and must be predicated on facts rather than conjecture or suspicion.

The United States Attorney for the Eastern District of Wisconsin in Milwaukee is the principal Federal law enforcement officer charged with responsibility for investigating and prosecuting Federal criminal offenses in your area.

It is my understanding that your complaint is being forwarded by the Criminal Division of the United States Department of Justice in Washington, D.C., to Assistant United States Attorney James M. Fergal in Milwaukee for an in-depth review. I suggest that you contact Mr. Fergal (414-291-1700) and provide him with any additional facts you consider relevant to your complaint.

On behalf of President and Mrs. Carter, I thank you for your confidence and support and extend to you their most solicitous concern. If I can be of any further assistance, please do not hesitate to contact me.

Sincerely,

Landon Kite

Landon Kite
Staff Assistant

Mr. and Mrs. James L. Grant
602 South University Avenue
Beaver Dam, Wisconsin 53916

Mr. and Mrs. James L. Grant
602 S. University Ave.
Beaver Dam, Wisconsin 53916

January 9, 1979

James M. Fergal
Assistant U.S. Attorney
517 E. Wisconsin Ave.
Milwaukee, Wisconsin 53202

Dear Mr. Fergal:

We are pleased you were able to come to Beaver Dam to meet with us and our son Scott last Wednesday while returning most of his trial transcripts. Since your schedule to return to Milwaukee by 4:30 rather limited our meeting, we wish to take this opportunity to express additional concern about the failure of the Bureau Of Biologics (BOB) to furnish Scott's attorneys with the requested Quadrigen records they needed in 1975, to properly try his case.

You indicated Parke Davis did not do anything illegal when they destroyed their files, but you did admit the Government is required to keep theirs. You further indicated you personally believed it was indeed possible that BOB could have misplaced them and you went on to compare it with the fact that records do get lost, even in legal offices that you have been involved with. In your view, despite it being an act of incompetence, it could not be considered a criminal act, unless, it could be determined they lost them on purpose.

Please allow us to remind BOB of the April 28, 1975, letter in which Mr. McKinnon states that Ray Crossley, the Freedom Of Information Officer at BOB said the Quadrigen records, had "vanished." The plain meaning, as well as the dictionary definition of "vanish" is "to disappear suddenly"; BOB here caused those crucial records to disappear suddenly within the very period Scott's attorneys requested them. That the records vanished was BOB's original claim and their language, not that of the Grants. It should be impermissible that the very Government Agency whose duty it is to protect citizens and consumers to make light of this nor at this late date to claim mere misplacement rather than their original claim that the documents had vanished.

The burden is unquestionably on BOB, to truthfully explain who is responsible for their sudden disappearance, and why. In view of the crucial importance to our totally disabled son, as well as to ourselves that these records be produced, BOB must be required to produce them and not permitted to escape this duty by a belated claim of misplacement. Government medical and scientific records are kept permanently in matters of this kind and this is particularly true where the subject matter in question has been involved in multiple catastrophic injuries to consumers and resulting litigation. This is essential for public safety.

We suggest if you are interested in learning what is going on so far as the present General Accounting Office (GAO) investigation is concerned, that you get in touch with Messrs. Jajokian and Tascar, who are actively engaged in the GAO's investigation of the BOB, that was requested by the five U.S. Senators, whose letter we furnished you a copy of. GAO's phone is: 301 - 443 - 2040

No responsible Government agency would or should have permitted Parke Davis to continue marketing a defective and harmful vaccine for a substantial period of time as was done here. Such an agency should have at the very least forced Parke Davis to recall the outdated vaccine and openly explained to the physicians the serious injuries it caused. BOB's demeanor in this matter cannot in justice be passed over or disregarded because whether by conspiracy, or gross incompetence or negligence BOB assisted Parke Davis to escape liability in this case. The Government's involvement makes it liable for the role it has played in the disastrous effects of Quadrigen from its original marketing through the lifetime of our son Scott and that of other victims.

You related to us in your interview that you had forgotten to bring with you BOB's letter of apparently on or about October 13, 1978, signed by a Mr. Cooper. We understand it contains information relative to the vanished records and other attempted explanations for the disappearance of the records. We request that you please send us a copy of this letter.

As you well know after personally seeing Scott, he is totally dependent and his ruined life and entire future are at stake. He will become eighteen years of age on June 4 of this year and the problems involved in his care are increasing. There is no time to spare in effecting as soon as possible adequate compensation and arrangements by which his future care can be provided, particularly after his parents are no longer available.

From what you have told us we do not believe BOB has furnished you with full and truthful information on this matter. We believe your investigation should continue and that it should include contacting the following persons, among others, for more authentic information.

Dr. J. Anthony Morris, a virologist formerly on the staff of BOB.
23 E. Ridge Road, Greenbelt, Maryland 20770 ... Phone: 301 - 474 - 5031

James S. Turner, a consumer attorney associated with the law firm, Swankin and Turner. 1625 I. St. N.W. Washington, D.C. 20006 ... Phone: 202 - 872 - 8660

We understand Mr. Turner has a very busy schedule and is required to be away frequently. He will be in Washington all of this week, but will be gone from January 18 until February 6.

We shall await receipt of the letter requested and your decision of procedure, upon having discussed the matter with Mrs. Kessler.

Sincerely,

Mr. & Mrs. James L. Grant

Mr. and Mrs. James L. Grant

Encl: 1/5/79 - W. Star, re: Dr. Morris

United States Department of Justice

UNITED STATES ATTORNEY
EASTERN DISTRICT OF WISCONSIN
517 EAST WISCONSIN AVENUE
MILWAUKEE, WISCONSIN 53202
TEL. 414-210-1700
FTS 362-1700

IN REPLY, PLEASE
REFER TO FILE NO.

January 12, 1979

Mr. Alfred Hantman, Chief
General Crime Section
United States Department of Justice
FTRI Building, Room 504
Washington, D.C. 20530

Re: Possible Obstruction of Justice
Our File No. 77-5921

Dear Mr. Hantman:

I am re-referring a citizen complaint to your Section. In September of 1977, Mr. Merkel of your office referred a possible obstruction of justice complaint to this office. A copy of that referral letter is enclosed for your convenience. Also, enclosed is a copy of a letter that Mr. & Mrs. Grant wrote the President and Mrs. Carter that predicated your referral.

This office is closing its file and investigation of this matter, having determined that the allegations are not substantiated by sufficient evidence with which to proceed. The letters enclosed are self-explanatory, however, the Grants complained of possible jury tampering, destruction of records by Parke Davis and destruction of records by the Food and Drug Administration. This office has made the determination that there is no evidence relative to jury tampering and further, any destruction of records by Parke Davis would not have been a violation of federal law. Further, a letter from Mr. Richard M. Cooper, Chief Counsel for the Food and Drug Administration answers the allegations of an intentional destruction of records by personnel with FDA. A copy of that letter is enclosed.

If an intentional destruction of records did occur within FDA, it would have taken place in Washington. Therefore, if the investigation is to continue, it should originate from the Department in Washington. The General Accounting Office (GAO) is currently conducting an audit of the

Bureau of Biologics, a Division of FDA. However, the supervisor of that audit, Mr. Jajokian, informed this office that GAO was not investigating the record retention policies of FDA.

Also enclosed, for your convenience, is a letter dated January 9, 1979 from Mr. & Mrs. Grant, again reiterating their claims.

Please be advised that this office is closing its file in this matter. However, if I can be of any further assistance to you, please so advise.

Very truly yours,

JOAN F. KESSLER
United States Attorney

JFK:bk

Enc.

cc: Mr. & Mrs. Grant

United States Department of Justice

UNITED STATES ATTORNEY
EASTERN DISTRICT OF WISCONSIN
517 EAST WISCONSIN AVENUE
MILWAUKEE, WISCONSIN 53202
TEL. 414 291-1700
FTS 362-1700

IN REPLY, PLEASE
REFER TO FILE NO.

77-[illegible]921

January 18, 1979

Mr. and Mrs. James L. Grant
602 S. University Avenue
Beaver Dam, Wisconsin 53916

Dear Mr. and Mrs. Grant:

Enclosed are copies of correspondence received by our office from the Chief Counsel of the Food and Drug Administration and a letter sent by our office to the Chief of the General Crimes Section of the Justice Department in Washington.

As Mr. Fergal indicated to you privately and in his letter to Mr. Hantman, our office has concluded further involvement in your son's case. Any possible intervention by the Justice Department hereafter will be initiated by the General Crimes Section in Washington, D.C. While I appreciate your disappointment in our inability to assist you directly, I sincerely hope that the aforementioned referral of your case to the Justice Department provides you and your son the assistance you desire.

Sincerely yours,

JOAN F. KESSLER
United States Attorney

By: Michael J. Trost

MICHAEL J. TROST
Deputy United States Attorney

MJT:gv
Enclosures

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
OFFICE OF THE SECRETARY
ROCKVILLE, MD. 20852

October 13, 1978

OFFICE OF THE
GENERAL COUNSEL

RECEIVED
OCT 16 1978
United States Attorney
Eastern District of Wisconsin

James M. Fergal
Assistant United States Attorney
Eastern District of Wisconsin
517 East Wisconsin Avenue
Milwaukee, Wisconsin 53202

Re: Quadrigen, Parke, Davis
Your File No. 77-5921.

Dear Mr. Fergal:

This is in response to your letter of July 13, 1978 requesting my assistance in obtaining from the Food and Drug Administration information concerning the loss of certain documents pertaining to a vaccine manufactured by Parke, Davis & Company, Quadrigen.

As your letter states, a request for documents was made by counsel on behalf of a child allegedly injured as a result of a series of vaccinations of Quadrigen in 1961. The request was made to the Bureau of Biologics, Food and Drug Administration, which has responsibility for licensing of such products pursuant to 42 U.S.C. 262. The request was only partially fulfilled, and it was determined that some documents had been misplaced or lost, including protocols for Quadrigen. Your letter sought the answers to two questions: (1) What attempts have been made by the FDA to find these documents? (2) How could these documents have been misplaced?

Upon receipt of your letter,I asked my staff to contact the Bureau of Biologics and obtain the full explanation., The responsible individuals at the Bureau (Mr. Ray Crossley and Mr.Bob Lee) provided my staff with a written explanation of the search efforts. After several discussions with Bureau employees concerning their written response, my staff reorganized that response. The contents of this letter are based on that response. I have not considered it necessary or apropriate for my office to make an independent investigation. What follows is the account of the Bureau's efforts to locate the documents as well as some background information on Quadrigen which the Bureau believes necessary to understand more fully what documents are missing. The contents of this letter have been rereviewed by the Bureau to assure that they are factually accurate and complete.

As Arthur Levine of my staff advised you by letter of August 14, 1978, vaccines came under the jurisdiction of the Food and Drug Administration in 1972. Prior to that time, the licensing of

vaccines was controlled by the Division of Biologics Standards, National Institutes of Health (DBS). In 1959, Parke, Davis and Company received a license from DBS for a multiple vaccine that included four components: diptheria and tetanus toxoids, an pertussis and polio vaccines. The product was named Quadrigen. Other drug companies received licenses as well for similar four-in-one vaccines. Prior to that time, there had been licensed three-in-one vaccines containing diptheria and tetanus toxoid and pertussis vaccine (DTP). In 1962, after developing problems with the potency of the pertussis component of Quadrigen, Parke, Davis changed the way in which the product was manufactured so as to avoid any future potency problems.

In 1959-62 Quadrigen was subject to the lot release requirements of the Division of Biological Sciences. (See, for example, present lot release regulation, 21 CFR 610.1). After a vaccine had been licensed and prior to any commercial distribution of the product, each lot of vaccine had to be tested for safety, potency, etc. Such tests were done by the manufacturer and by DBS as well. The manufacturer would submit a "protocol" for release of a lot of vaccines. That protocol would identify the vaccine manufactured, and would contain all necessary test results required for release. For a particular lot of polio vaccine, the protocol might be quite voluminous. However, as will be explained, the protocol for Quadrigen would have been, in comparison, quite small since it only referenced earlier protocols for separate lot releases fo DTP vaccine and polio vaccine.

Due to DBS requirements concerning dating periods (the time limits for commercial use), licensed manufacturers of this type of quadruple vaccine would utilize portions of lots of DTP and polio vaccine that had already been separately lot released. The point at which they combined these two products to form the four-in-one vaccine was considered by DBS to be the point of manufacture. Parke, Davis or any other manufacturer then would send in a protocol for Quadrigen, which would merely reference the earlier lots (by number) of DTP and polio vaccines that were used to make the four-in-one vaccine. Thus, the majority of testing data for Quadrigen would not be in the final Quadrigen protocol, but rather in the earlier protocols for DTP and polio vaccines.

The final Quadrigen protocol, however, was (and still is) the key to the majority of the data generated. It is conveivable that the testing data for the DTP and polio components of Quadrigen for 1959-62 are in government files but it would be impossible to tell which lots were utilized by Parke, Davis to make the Quadrigen. A copy of a Quadrigen protocol for 1962 is attached to give you an idea of the volume of the documents involved. This protocol, along with numerous other documents, correspondence, etc. was found and provided to counsel at the time of the initial request.

In the fall of 1974 and then again on March 29, 1975, counsel for Scott Grant of Beaver Dam, Wisconsin, contacted the Bureau of Biologics. Counsel advised the Bureau that he represented plaintiffs in a law suit against Parke, Davis and Company. The letter of March 29, 1975 set out a series of documents that counsel was requesting in order to prepare for a trial that was to occur in June, 1975. (A copy of that letter is attached). The Bureau of Biologics treated the letter as a request for documents under the Freedom of Information Act. As a result, the Bureau's FOI Officer, Ray Crossley, was put in charge of retrieving the requested documents. Prior to a meeting in Washington, telephone conversations between counsel and Mr. Crossley led to a greatly restricted request for documents. The documents which counsel was primarily interested in (protocols) concerned the manufacture and lot release of Parke, Davis' Quadrigen manufactured during 1959-62 since his client received his vaccinations in the fall of 1961. Counsel was interested as well in files, correspondence, adverse reactions and complaints for Quadrigen generally, not limited to 1959-62. Once the request for documents was narrowed as to protocols, Mr. Crossley began the task of locating them.

Mr. Crossley initially contacted Bob Lee, Director, Document Control Center, Bureau of Biologics and requested him to look for the documents pertaining to Quadrigen. Mr. Lee and/or his associate Harold Rusten looked in the two buildings that house the Bureau of Biologics on the National Institutes of Health Campus (Building 29 and 29A). Next, Mr. Lee and Mr. Rusten obtained records stored at the Federal Records Center, Suitland, Maryland 1/. When these attempts by Mr. Lee and/or Mr. Rusten did not uncover the protocols for the relevant time period, Mr. Crossley became involved in the actual search. Some correspondence and data concerning Quadrigen were found and given to counsel 2/.(A complete set of the records supplied to counsel in 1975 accompanies this letter.

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1/ All records that are either five years old or deemed inactive are boxed, indexed and shipped to the Federal Records Center for storage. Mr. Lee maintains the index of boxes shipped for storage, and they can be retrived from the Federal Records Center by use of accession numbers. The accession numbers coincide with classes of documents, years and manufacturers.

2/ The documents consisted of reports and correspondence pertaining to Quadrigen. There do not appear to have been any adverse reaction reports among these documents. The DBS regulations in effect during this time period required the

Mr. Crossley made two visits to the Federal Records Center, along with Mr. Rusten,in an effort to locate the missing documents. On these occasions, utilizing the accession numbers maintained by Mr. Lee, the personnel at the Federal Records Center were asked to retrieve all boxes of protocols that the Bureau of Biologics had stored there. They also requested boxes that related to correspondence or any other material that might have been even remotely related to protocols. All of these boxes (an accurate estimation of their number is difficult to make) were reviewed item-by-item in an attempt to locate the desired documents.

When these searches failed to locate the protocols, Mr. Crossley and aides spent several days searching once again through all the storage areas at the Bureau of Biologics (Buildings 29 and 29A). This search involved reviewing the contents of several hundred stored boxes, whether or not they indicated the contents might contain protocols. This search included not only the usual record storage areas but also the attic and sub-basements, so that Mr. Crossley could be assured that no boxes had been stored in areas other than normal. Mr. Crossley spent approximatley one full work week attempting to locate the documents. In addition, Mr. Lee and his associate expended approximately the same amount of time in the effort. As you are aware, there was a Congressional inquiry into

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Footnote continued

2/ firm to maintain records in their files of "unfavorable reactions"for review and copying by DBS investigators (now 21 CFR 600.12 and 600.22). These regulations did not require the firm to submit reports of "unfavorable reactions" to DBS.

Drug firms are required to submit adverse drug reaction reports to the Bureau of Drugs, Food and Drug Administration. Counsel's 1975 FOI request to the Bureau of Biologics recognized this fact and sought "any and all data from the drug reaction group of the Bureau of Drugs." As a result my staff contacted the Division of Drug Experience, Bureau of Drugs, to determine their response, if any, to counsel's 1975 request. Their records could not be located for requests for adverse drug reactions in 1975 so they checked their computer to determine whether they had any adverse reaction reports for Quadrigen at all. They did not find any adverse drug reaction reports for Quadrigen in their computer and thus a response from them in 1975 would in all likelihood have indicated that fact. It should be recalled that until 1972, vaccines, such as Quadrigen, were not regulated by the Food and Drug Administration. Thus, in the normal course of events, firms manufacturing vaccines prior to 1972 did not submit information to the Bureau of Drugs.

the loss of the documents and, at that time, Mr. Crossley repeated his search through the Bureau of Biologics and the Federal Records Center, but to no avail. During Mr. Crossley's search he also inquired of other Bureau of Biologics employees whether they knew of the location of these documents.

Your second request for assistance asks me to speculate as to what must have happened to the missing documents. Neither Mr. Crossley nor anyone else connected with this matter can explain the disappearance. No one from the Bureau has advised either Mr. Crossley or my staff that he knows where the documents are now or how they have been lost.3/ Obviously, the Bureau of Biologics, as did the Division of Biological Sciences, generates and receives a massive amount of paper. There is a system of document retention employed by the Bureau of Biologics, as well as the rest of government. Older documents (over five years old) or those deemed inactive are kept at the Federal Records Center in Suitland, Maryland. I am advised that periodically (every twenty years) the Center requests the Bureau to review documents and destroy those no longer deemed worthwhile to save. The Quadrigen documents may have been inadvertently destroyed during one of these reviews. Also, when the Bureau of Biologics came into existence in 1972, there was an attempt on the part of Bureau personnel to "houseclean" and destroy unnecessary documents and papers. The documents may have been destroyed at that time. A third possible explanation lies in the fact that, since there was a great deal of litigation concerning these products especially during the 1960's, the documents could have been removed from their normal retention sites, utilized in a discovery session, depositon, etc. and then inadvertently not returned to their regular location. As I discussed earlier, since the Quadrigen protocols themselves may have been very small in comparison to the larger protocols for the lots of DTP or polio vaccines utilized, it is not hard to visualize such documents being misplaced once they had been taken out of the normal flow of document retention. Again, however, this is mere speculation since the Bureau has no knowledge of what actually happened to the documents.

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3/ Mr. Crossley is aware of four other requests pursuant to the Freedom of Information Act for Quadrigen documents. Two requests were made and then cancelled; one request was for package inserts and one was for general information. This last request will be filled with the same data being submitted to you.

There are several related points to be made regarding the loss of these documents. First, as noted earlier in my letter, the search for protocols was limited to the period 1959-62. Your letter states that plaintiff's attorneys were advised that protocols covering 1959 to 1968 for Quadrigen were missing. That is partially incorrect. Several Quadrigen protocols for 1962 were in fact turned over to counsel for Scott Grant. Other protocols after 1962 may or may not be missing, but the Bureau was not asked to search for them. A second concern expressed by Bureau of Biologics'employees deals with the relevancy of these missing protocols in light of the fact that, apparently, at trial plaintiff was unable to identify Parke, Davis' Quadrigen as the product received by the child. This consideration is raised by a newspaper article provided by the Bureau of Biologics (copy attached) and also by statements by Bureau employees who say that counsel for the child stated to them during meetings prior to trial in 1975 that he did not know which company's vaccine had been given to the child. This is obviously a separate issue from the apparent loss of the documents, although Bureau employees are puzzled over the relevancy of these protocols since they would not have aided in establishing that the child in fact received Quadrigen. In addition, the Bureau records which include all lot releases of Quadrigen during the relevant time periods of 1960-61 show that, based on dating period requirements, there would have been no Quadrigen legally in commerce during the time period when the child was vaccinated. A copy of the log book indicating this fact was given to counsel prior to trial in 1975.

I hope this information has been of assistance to you in answering the questions you raise. If I can be of any further assistance to you in your inquiry, please let me know.

Sincerely,

Richard M. Cooper
Chief Counsel
Food and Drug Administration

Enclosures

UNITED STATES DEPARTMENT OF JUSTICE

WASHINGTON, D.C. 20530

Address Reply to the Division Indicated and Refer to Initials and Number

ALH:EJW:pa

16 MAR 1979

Mr. and Mrs. James L. Grant
602 South University Avenue
Beaver Dam, Wisconsin 53916

Dear Mr. and Mrs. Grant:

This letter is in response to the letter dated January 12, 1979, of Joan P. Kessler, the United States Attorney for the Eastern District of Wisconsin, as well as your letter of February 2, 1979. As you will recall, your original letter to President Carter concerning alleged obstruction of justice in a Federal civil trial was forwarded to the Criminal Division of the United States Department of Justice. The Criminal Division in turn forwarded your complaint (alleging possible jury tampering and obstruction of justice in connection with your Federal civil trial in Milwaukee involving your son Scott's tragic injuries and illness against Parke, Davis and Company) to the United States Attorney for the Eastern District of Wisconsin, the principal law enforcement officer with responsibility for investigating and prosecuting federal criminal offenses in your area.

As you have been advised, the United States Attorney, after an in-depth review and careful evaluation, determined that the allegations of possible jury tampering and obstruction of justice in connection with your civil suit against Parke, Davis and Company were not substantiated by sufficient evidence with which to proceed. In her letter, the United States Attorney stated as follows:

> "This office has made the determination that there is no evidence relative to jury tampering

and further, any destruction of records by Parke Davis would not have been a violation of federal law. Further, a letter from Mr. Richard M. Cooper, Chief Counsel for the Food and Drug Administration answers the allegations of an intentional destruction of records by personnel with FDA."

The Criminal Division has reviewed this matter very carefully, including consultation with the United States Attorney's office in Milwaukee, and concurs with the opinion of the United States Attorney that the allegations are not substantiated by sufficient evidence with which to proceed. A destruction of records by Parke, Davis and Company without sufficient evidence of the requisite criminal intent to influence, intimidate or impede the federal civil action is not a violation of the federal obstruction of justice law. Also, with respect to the allegation of intentional destruction of records by personnel with the Food and Drug Administration (FDA), we likewise concur with the United States Attorney that the letter from Mr. Richard M. Cooper, Chief Counsel for FDA, answers this allegation. Additionally, it is noted that there is no apparent corrupt motive for the FDA to have intentionally destroyed these records. There is no factual basis to justify continuing this investigation of alleged intentional destruction of records by the FDA in Washington, D. C.

It is noted that in June 1975 a jury in the United States District Court for the Eastern District of Wisconsin rendered a verdict for the defendant Parke, Davis and Company in your civil action. The Court of Appeals for the Seventh Circuit and the United States Supreme Court have concluded that your appeal lacked merit on the basis of the record made in the District Court. Although you are certainly disappointed with and may disagree with the jury's verdict and the decisions of the Federal appellate courts, we can assure you that the integrity of our Federal appellate courts is beyond reproach.

Although only you can truly appreciate the tragedy you and your son have suffered, we empathize with you. We trust that you will appreciate our responsibility in the Criminal Division of the Justice Department to perform our duty and properly utilize our resources in investigating violations of federal criminal law within our jurisdiction and prosecuting the violators when justified and warranted by sufficient evidence. Based on our review of the file in this matter, we conclude that no further investigation by the Criminal Division is warranted.

Sincerely,

ALFRED L. HANTMAN, Acting Chief
General Litigation and
Legal Advice Section
Criminal Division

Edward J. Walsh

By: EDWARD J. WALSH
Attorney

Senator HAWKINS. Thank you so much, Mrs. Grant.

Now, we will turn to Mrs. Williams. Do you have a statement?

Mrs. WILLIAMS. Yes.

Senator HAWKINS. I understand that your group's title is Dissatisfied Parents Together. Is there any similarity to the initials, DPT? Is that where you got your title?

Mrs. WILLIAMS. Yes. We chose to have the name of our organization begin with the letters DPT so that people would recognize it.

Senator HAWKINS. How did you form that organization?

Mrs. WILLIAMS. On April 19, 1982, a local station ran a documentary on the DPT vaccine. In response to the show, I called the station to see if there was something being done by local parents. They took my name and number and said they would give it out to interested callers. Three other parents in the area did the same thing, and at the end of the day, we contacted each other. We all four had been swamped with telephone calls from parents. We compared notes and found that we were all hearing basically the same stories. Generally, we found that most parents did not know the pertussis vaccine had severe side effects. Most parents said they had not reported their child's reactions to the DPT shots because their doctors had not told them to watch for severe reactions.

Some parents reported that their children had mild reactions to the shots, such as temperature or fussiness. Some reported moderately severe reactions such as high-pitched crying, unconsolable screaming for long periods of time, and some reported very severe reactions, such as convulsions and brain damage. Sadly enough, several callers reported that their babies had died within 48 hours of the vaccine.

The reactions were fairly evenly split between the four shots. In other words, some children reacted to the first shot, but some did not suffer damage until the third or fourth shot. Many of these parents were shocked after seeing the documentary and remembering that their children had had similar severe reactions. They suddenly realized that their child's convulsions, retardation or death may have been caused by the pertussis vaccine. Again, most parents had no idea that the shot could cause such reactions.

We began to wonder exactly how many children in America had been affected. At this point, we decided we needed to organize Dissatisfied Parents Together, to collect and distribute information to parents about the pertussis vaccine, particularly after we discovered there were conflicting statistics, and no consensus of opinion within the medical community regarding the safety of the vaccine. We wanted to find answers to several questions.

No. 1, although several studies have been done, why has the Government had a limited research program dealing with adverse effects of the vaccine?

No. 2, why hasn't a safer vaccine been developed and we understand that they are working on one.

No. 3, why haven't high risk children been identified?

No. 4, why haven't physicians been required to report adverse reactions to a central recordkeeping agency?

No. 5, why haven't physicians and parents been better informed about the possible reactions to the pertussis vaccine?

No. 6, should the States mandate that the present pertussis vaccine be given to all children who attend school?

And No. 7, should there be a compensation program for children who have been retarded or seriously disabled by the pertussis vaccine?

Senator HAWKINS. What were the circumstances surrounding your own son's DPT immunization, Mrs. Williams?

Mrs. WILLIAMS. My son, Nathan, is 16 months old, and he has had four DPT shots. The first three, he had a slight fever and fussiness. I was told by my pediatrician to expect this, nothing else. After the fourth shot, he experienced severe, high-pitched screaming for 6 straight hours. There was nothing we could do to console him. When I reported this to my doctor she told me that he should never have the vaccine again, that this was a contraindication.

Now, I did not know at the time that severe, high-pitched screaming may have been an indication that his brain was swelling and could lead to brain damage. In addition, I have a history of seizures, as do other members of my family, and I realize now that Nathan was a high risk child and should never have had the vaccine in the first place. And I would like to make a comment. One of the gentlemen said earlier that 1 in 2,000 children have seizures. I feel if I had known that, having a seizure problem myself, I would never, ever have let him take that chance, because I know what it is like to live with a seizure disorder.

His reaction was not reported to the drug manufacturer.

I am joined with my cofounders by a love for our children and the common desire to keep our children healthy.

[The following was received for the record:]

This is a statement of purpose by the Organizing Committee of Disatisfied Parents Together (DPT). Our reason for organizing stems from a common concern for the health and well-being of all children. Our specific goals are:

* to effect in-depth research and a comprehensive study of the side effects and effectiveness of the pertussis portion of the DPT immunization

* to effect mandatory reporting by physicians of adverse reactions to the DPT immunization to a central record keeping agency

* to promote better education among physicians and parents as to the possible side effects of the pertussis vaccine

* to identify high-risk children

* to effect the development of a safer vaccine

* to promote public debate on whether or not the pertussis vaccine should ever be a mandatory requirement to attend school

* to promote the adoption of a compensation program for children who have been retarded or seriously disabled by the pertussis vaccine

* to effect the development of treatment centers and social service programs that will aid children who have been damaged by the pertussis vaccine

Senator HAWKINS. Thank you, Mrs. Williams, for addressing the concern of parents. We also commend you for the action you have taken so rapidly after being informed by the media. Your testimony has been very welcome and very helpful.

Mr. Preiser, we welcome you to this panel today. You are an attorney from Charleston, W. Va. Could you tell us what problems are encountered by families if they try to seek recovery for damages to their children as a result of adverse reactions to vaccinations?

Mr. PREISER. Thank you, Senator.

First, I think one of the problems that is reflected here today—and if I might, I do not think that some of the testimony given by the first panel can go unanswered to some degree, because I think that is particularly what is reflective of many problems. I keep hearing the question from you, Senator, as to "the" vaccine, the pertussis vaccine. I did not hear anyone mention the fact that there is more than one type of pertussis vaccine. Every manufacturer makes it differently—at least, this is what we have been able to determine in depositions and other lawsuits.

Senator HAWKINS. How many manufacturers are there, to your knowledge?

Mr. PREISER. We do not know now, at the present time. Some have gotten out of the business. Some have sold. There are, I would think, three or four at the present time, at least, in the United States. There are other European manufacturers, and that is a very important factor, because there have never been any studies, to the best of our knowledge, performed by the Government or required by the Government or by any pharmaceutical manufacturer, as to whether or not one vaccine is better than the other. What if we have vaccine by manufacturer A that has never harmed anyone, but vaccine by manufacturer B that harms numerous individuals? No study has ever been performed. There has never been a comparison to the best of our knowledge as to whether or not the vaccines are the same—we know they are not—but what the differences are in the vaccines, whether they be in Europe or in America. We do not know whether the British vaccine is the same as the Swedish vaccine, or whether the Swedish vaccine is the same as the West German vaccine. I believe no one has ever told your investigative committee what the differences are, either. The reason they have not told them is because the Government has been negligent in not requiring such studies. That is one problem.

A second problem. Where are all the studies as to the statistics of individuals who have been hurt? We hear this gentleman say 1 in 100,000. Does that mean 1 in 100,000 doses? That may mean 1 in 25,000 people, because every person gets four vaccines. Now, that is very interesting because, I suggest, those statistics may not be right, because there is no completely objective diagnosis of encephalopathy or problem from DPT. It is a diagnosis of exclusion; when they cannot find anything else out, they say this must be from DPT because of the time relation between the problem that occurs and the vaccination itself. One cannot look at a blood sample, for example, or one cannot look at a spinal tap, for example, and see that one has a reaction or an encephalopathy or some other problem from DPT. It is a diagnosis of exclusion.

And they tell you today, the Government representatives, that they rely on other committees, the Red Book Committee, for example. I need to tell you, Senator, a story about the Red Book Committee. A group of physicians, supposedly the best in our country, got together in 1974 to determine what the contraindications were to pertussis. They did not know a thing about the screaming and the crying that the gentleman told you about over here as a contraindication—this was 1974 when they had their meeting, and they have it every 2 years or so—they did not know a thing about it, or at least did not include it in their listed contraindications. They had not studied all the literature, and the literature was replete with screaming syndrome from Europe, from major medical journals in Europe, some in the United States, some textbooks; they did not know anything about it. And the reason they did not know anything about it is because Dr. A has two or three reactions, Dr. B has two or three, Dr. C two or three, and among them, they do not think it is very significant. The problem is that they all report it to the manufacturers, and the manufacturers have a duty to know what the problems are, but the Government does not require the manufacturers to tell anybody else, and the Government does not require any independent studies. The Government does not require the manufacturers to make any independent studies. And then the Government comes in here today and accuses NBC of journalistic malpractice in the show, and I do not think that can go unanswered because no one from NBC is here to answer it. I am not from NBC, but I can guarantee this committee, I gave enough information to NBC myself, along with a number of other individuals that I know about, that they were well-informed in their show. They probably knew more than the Government ever knew prior to 1978. The malpractice has been on the other foot, on the part of the Government, since 1978, in the failure to take accurate statistics and make accurate studies. That is one problem.

If I am not boring the committee, let me move on for just a moment to another, major problem, and that is the statute of limitations problem.

Many, many of these parents have not incurred these problems within the last 2 or 3 years, when we do have some awareness of the problems of pertussis finally. Why it has come about in the last 2 or 3 years, I really do not know. But many of the problems occurred 10, 15, even 20 years ago. Now, in order to sue the Federal Government, as the Senator may be aware, one has to follow the requirements of the Federal Tort Claims Act. There is a 2-year statute of limitations after one knows of the problem that one has in which to bring a lawsuit. Incredibly enough, Senator, this does not even allow a young child, who has no idea what his or her rights would be at the tender age of 2, of course, to wait until that child reaches the age of majority to be able to find out whether he or she is going to bring his own lawsuit. If a parent does not bring a lawsuit within 2 years for a child, that child's rights are waived and barred. That is a major problem, because most States have particular statutes that allow children to bring a lawsuit to protect their own rights, 2 years after the date that they have turned whatever the age of majority is of that State—18, 20, 21—I think

Florida does not, however. I think Florida actually follows the Federal guidelines.

But that is a major problem among parents who have children who are tremendously brain damaged and are incurring incredible expenses for private education, private nursing care, and have no recourse for that child now, or perhaps not even for themselves now, against a Government agency, if a Government agency gave the shot, which many did when they should not have. There are numerous, numerous cases of doctors within the Government agencies giving those shots when they should not have—and no lawsuit; no recovery, no possible remuneration for the parents in that situation.

If one wants to bring a lawsuit against the FDA, it cannot be done, for those hundreds of parents that we know about. And I know NBC has received thousands of calls, hundreds of letters, of parents who are experiencing these problems.

So the statute of limitations is one major problem against the FDA or against any Government agency, whether it be the Army that gave a shot improperly at these clinics which they have, or not. It is something which needs to be looked into, perhaps. These parents are not going to be able to take care of these children. The parents are going to die, and these children are going to be forced to enter an institution somewhere, where they are not going to be taken care of properly when, if it is someone's fault that the children are in a condition like this, they ought to be able to be taken care of or have the money to be taken care of by private individuals at their own homes.

I hope that answers part of that question.

Senator HAWKINS. Thank you. In your opinion and with the experience that you have, do the warnings accompanying the vaccine adequately inform individuals of any risk?

Mr. PREISER. If I might, there are two areas of warnings. There are warnings that go to physicians with regard to certain drugs, not vaccines—tablets, capsules. Those warnings, the theory is, are to be given by the physician to the patient when the physician writes a prescription, and a manufacturer of the drug is not required, and should not be, and is not under any law required to give anything in particular to the recipient of the drug, because the intermediary has that responsibility.

We have a different situation with vaccines, Senator, where many vaccines are given in clinics without doctors—especially this pertussis or DPT vaccine, which is required in so many States, and almost all children get it—in rural areas, they go into a clinic, they get it from a nurse. In all of the U.S. Army clinics, they go into a clinic, they get it from some nurse's aide, and not from a doctor. In that situation, Senator, there should be a warning that is given specifically to the parent of the child, warning that parent as to what reactions might occur, because unfortunately, so many of our doctors do not know today what those reactions are; also, giving the parent some freedom of choice in this country as to whether or not the child should receive a vaccine that at least today, as the Senator can see, there is some great controversy as to whether or not it should be given. And I am not here to argue one position or the other, only that one be properly warned.

I understand the Government at least, perhaps, does now give those personal warnings. That has only been in the last 2 years. Where were they for the last 10 or 15 years when the people should have been getting it? The manufacturers of the vaccines do not give it out as a matter of course.

So my answer to you has to be that the warnings given to the parent are probably not enough in this day and age, whereas the warnings given to the doctors and contained in the literature probably are enough.

Senator HAWKINS. We really appreciate all of you participating. Mr. Preiser, you have been most helpful to us in understanding some of the legal problems faced by parents. I understand that you and your wife are expecting a baby any minute, and we deeply appreciate your taking the time to come here and testify before this subcommittee. It has been most helpful.

We would like to wish you and your wife well. We had a 9-pound, 6-ounce grandson yesterday morning.

Mr. PREISER. I understand that. Congratulations to you.

Senator HAWKINS. Thank you. We will excuse the panel at this time. Mrs. Grant?

Mrs. GRANT. I have one more thing I would like to say. Dr. Foege—or I do not know which of the gentlemen mentioned it—this form that is given out in public clinics. That is fine. They are better informing those kids who get their shots at the public clinics now. That is only really fairly recent. But the private physician does not give you anything, and that is where most of the infants are really and truly vaccinated. And this is such a crucial thing.

Senator HAWKINS. We appreciate that information.

Mrs. GRANT. And another thing I would like to just quickly add, the Government has had this information for 12 years at least, that this pertussis vaccine is just not very good. I mean, they have had details on it. Why haven't they done something about it? It took NBC to really air these things so that they woke up. That is terrible.

Senator HAWKINS. We agree, and we are going to have some recommendations for the agencies that we do supervise. As you say, the taxpayers really are the final employer. We appreciate the testimony of concerned citizens. Mrs. Williams, do you have a final statement?

Mrs. WILLIAMS. I would like to add one more thing. We do not believe that our choice must be to risk the death or brain damage of our children from an inadequate pertussis vaccine, or risk the death or brain damage of our children from a whooping cough epidemic. We believe that American physicians, scientists, and drug manufacturers should long ago have heeded the warnings of the side effects of the pertussis vaccine and made more serious efforts to develop a safer vaccine.

It is for the lives of our children of today and the lives of our children of tomorrow that we plead with doctors and this oversight committee to stop ignoring reports of the dangers of the vaccine and act now. We must not continue to jeopardize the lives of children who have, by most State laws, no choice at all.

Senator HAWKINS. Thank you so much for coming.

We will excuse this panel at this time.

As our final panel, we will call Dr. Alfred Munzer of the American Lung Association and a physician with the Washington Adventist Hospital; Dr. Robert Parrott, director of Children's Hospital; Dr. Vincent A. Fulginiti, chairman of the Committee on Infectious Disease for the American Academy of Pediatrics, and Dr. Shirley Fannin, chief of acute communicable disease control for the County of Los Angeles Department of Health Services.

We welcome you here today doctors. I appreciate all of you taking time out of your busy schedules. We are going to begin today with Dr. Parrott. I understand he has an appointment this afternoon, so we will start with him.

**STATEMENT OF ROBERT H. PARROTT, M.D., DIRECTOR, CHILDREN'S HOSPITAL, WASHINGTON, D.C., VINCENT A. FULGINITI, M.D., CHAIRMAN, COMMITTEE ON INFECTIOUS DISEASE, AMERICAN ACADEMY OF PEDIATRICS, TUCSON, ARIZ., SHIRLEY FANNIN, M.D., CHIEF, ACUTE COMMUNICABLE DISEASE CONTROL, COUNTY OF LOS ANGELES, DEPARTMENT OF HEALTH SERVICES, AND ALFRED MUNZER, M.D., AMERICAN LUNG ASSOCIATION, WASHINGTON ADVENTIST HOSPITAL, TAKOMA PARK, MD.**

Dr. PARROTT. Thank you, Senator. I was asked primarily to comment on the NBC television program of April 20, which raised questions about the use of the pertussis or whooping cough component of routine childhood immunization. That coverage, as has already been mentioned, gave heavy and emotional emphasis to possible neurologic reactions to the vaccine, and it was suggested that physicians were not aware of or not disclosing to families the potential risks.

The fact is that public health and pediatric leaders in the country have carefully reviewed the potential risks versus the benefits of the pertussis vaccine, and concluded that routine immunization should be continued.

Also, many feel that overemphasis on the risks, such as was done in that program, might lead to a situation as has now occurred in Great Britain—and quoting from the British journal Lancet of May 23, 1981—where "More children died of pertussis in the 1977-79 epidemic than would at latest risk estimates have been severely damaged by vaccination." The current view, which was distorted on the NBC program, of the British Government is that the "balance of risk is in favor of continued vaccination, with stringent attention to contraindications."

I think one of the problems in our country is that whooping cough vaccine use has been so effective that young families and young health workers, as you indicated previously, Senator, are not familiar with the disease. Perhaps somehow, we need to turn the clock back to the twenties or thirties, when 100,000 to 250,000 cases were reported a year. Perhaps we need more testimony from grandparents who remember, as you indicated you remember, what whooping cough was like.

Let me briefly review that. There is an early catarrhal, or cold-like stage, with symptoms of a cold—sneezing, watery eyes, cough—and a low-grade fever. And it is important to note that

during this stage, when the responsible germ is growing and multiplying and most likely to be spread to other people, including young infants in the family, you cannot make the diagnosis. It is not easy to make. You can suspect it, but during the cold-like stage, it is like any cold, and it can spread around.

Senator HAWKINS. You cannot make the diagnosis; is that right?

Dr. PARROTT. Not at that point.

There is then a paroxysmal, or whooping, stage. And let me just read a description of the disease from one of the standard texts, and I have a couple of pictures here, but since you say you have seen the disease, I do not know whether you need them; but perhaps some of the others would like to see them.

Senator HAWKINS. Thank you.

Dr. PARROTT. "The cough now comes in explosive bursts. A series of 5 to 10 or more short, rapid coughs is given on one expiration and is followed by a sudden inspiration associated with a characteristic, high-pitched, crowing sound, or whooping." So, the child is going "cough, cough, cough, cough, cough . . . whoop" and is close to strangling. "The child's face becomes red or blue, the eyes bulge, the tongue protrudes, and the whole expression is anxious or utterly miserable." And there is a picture in this book, which perhaps you would like to share, of a child in this stage.

"A number of these attacks may be grouped together until the child succeeds in dislodging a plug of mucous. Vomiting frequently follows. Then the child often appears listless, dazed, or out-of-touch. He is likely to sweat profusely and show swelling of the face. During the first 1 or 2 weeks of this stage, the attacks get worse and worse. They continue for 1 to 3 weeks." I am ending a quote from that textbook at this point.

Then there is a convalescent phase, weeks to months, and some children will develop recurrent coughing attacks, complete with whoop and vomiting, after other infections for 1 or 2 years thereafter.

The most common and usually the most severe complication is pneumonia, especially feared in infants under 1 year of age. This can lead to chronic lung problems, with sacs of pus or bronchiectasis, collapse of the lung, atelectasis, or air-trapping, emphysema. This latter is a common autopsy finding and probably exists in the lungs of many patients. Convulsions may result from the loss of oxygen during severe paroxysms and from small bleeding spots in the brain. Bleeding can occur in the eyes, the nose, and the skin, as well as the brain. And here is a picture of bleeding in the eyes and a lesion that can occur in the mouth when the child is coughing severely during the paroxysmal phase.

The death rate has been mentioned earlier and is about 10 per 100,000 cases, and most deaths occurred in very young infants, those likely to be exposed by older children, not immunized. This severity in young infants is why it is recommended that pertussis immunization begin as early as 2 months of age.

I want to quote again from one of the respected texts:

> The severity of pertussis is not commonly appreciated. The greatest danger from it occurs in infants. When the outlook for an individual patient is assessed, the presence of complications has an important bearing on his future health, as well as on his immediate survival. Interstitial pneumonia that is unresolved or slow to resolve,

and persistent atelectasis, are common danger signals of the pus sacs or bronchiectasis. The onset of asthma has been observed to follow whooping cough. Cerebral manifestations are ominous. Sudden death from asphyxia due to obstruction of the airway may occur in uncomplicated cases. This emphasizes the vital importance of close nursing supervision.

That is ending quote, again from the text, Krugman and Katz, Infectious Diseases of children.

So much for what whooping cough is; I want to and call your attention to a recent analysis of the risks and benefits of pertussis vaccine which was in the "New England Journal of Medicine," volume 301, page 908, in 1979.

[The article referred to follows:]

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The New England Journal of Medicine (ISSN 0028-4793) is published weekly from editorial offices at 10 Shattuck Street, Boston, MA 02115. Subscription price: $25 per year. Second-class postage paid at Boston and at additional mailing offices.
POSTMASTER: Send address changes to 1172 Commonwealth Avenue, Boston, MA 02134.

NEJMAG 301(14) 737-796 (1979)

# PERTUSSIS VACCINE — AN ANALYSIS OF BENEFITS, RISKS AND COSTS

JEFFREY P. KOPLAN, M.D., M.P.H., STEPHEN C. SCHOENBAUM, M.D., M.P.H., MILTON C. WEINSTEIN, PH.D., AND DAVID W. FRASER, M.D.

**Abstract** Using decision analysis, we estimated the benefits, risks and costs of routine childhood immunization against pertussis. Without an immunization program, we predict that there would be a 71-fold increase in cases and an almost fourfold increase in deaths (2.0 to 7.6) per cohort of one million children. With a vaccination program, we predict 0.1 case of encephalitis associated with pertussis and five cases of post-vaccination encephalitis; without a program, there would be only 2.3 cases of encephalitis associated with pertussis. Community vaccination would reduce by 61 per cent the costs related to pertussis. Our analysis supports continuation of vaccination in routine childhood immunization programs, but suggests the need for more reliable data on complications from the vaccine, further study of the epidemiology of pertussis and development of a less toxic vaccine. (N Engl J Med 301:906-911, 1979)

THE value of pertussis vaccine has been questioned recently, particularly in the United Kingdom.[1-3] The decreasing incidence of pertussis, and concerns about the degree of efficacy of the vaccine and about vaccine-associated complications, have led to some proposals to curtail pertussis vaccination. However, a formal benefit-risk analysis has not been reported.

We used existing clinical and epidemiologic data to: *(1)* itemize and quantify the principal variables that contribute to an assessment of the risks, benefits and costs of pertussis vaccination programs; *(2)* determine which variables are most important to a decision; and *(3)* indicate for which of these variables better epidemiologic data is needed. We then compared benefits, risks and costs to evaluate whether routine immunization should be continued.

## ANALYTIC MODEL

The risks of pertussis are measured by the expected number of cases and complications (including permanent disability and death). The benefits of vaccination, therefore, are considered to be the number and costs of cases and complications that can be prevented by vaccination. The risks are the expected number of major and minor reactions and their costs.

### Decision Tree

The technic of decision analysis facilitates a comparison of outcomes of alternative strategies.[4] Figure 1 is a decision tree about whether or not to include pertussis vaccine in a community-wide vaccination program. The proportion of persons experiencing each outcome at the tips of the tree (right side of figure) is equal to the product of the probabilities along the branches leading to that outcome. The tree thus allows an estimate of the number of persons in a cohort who experience each outcome (i.e., the number of cases, hospitalizations, pertussis-related complications and deaths, and vaccine-related complications and deaths) and permits a comparison of alternative vaccine strategies for their effects on morbidity, mortality and aggregate medical-care cost.

The probabilities assigned to the branches at the chance nodes were based, whenever possible, on published data. When published studies were inadequate or nonexistent, we made assumptions and subjected them to sensitivity analysis. When it was necessary to make estimates, we purposely tended to overestimate the risks and underestimate the benefits of the vaccine. Thus, we assumed that partially vaccinated children had no immunity and developed disease with the same frequency and severity as unvaccinated children. We considered fully vaccinated children who nevertheless became ill to have had the same risks of disease complications as the unvaccinated. We analyzed the hypothetical experience of a cohort of one million children from birth to six years of age because virtually all pertussis mortality and severe morbidity occur in this age group and because most immunization programs do not recommend pertussis vaccine after the age of six.

### Decision to Vaccinate (Point 1, Fig. 1)

We evaluated the use of "triple" vaccine — diphtheria and tetanus toxoids and pertussis vaccine (DTP) — in children two, four and six months of age, with a booster dose at 18 months, as advocated by the American Academy of Pediatrics.[5] We compared this policy with one in which the pertussis component would be dropped from the vaccine. Children were not considered immunized until six months old, and were either "vaccinated" (three doses by six months of age and four doses by 18 months of age) or "unvaccinated."

From the Office of Program Planning and Evaluation and the Bureau of Epidemiology, Center for Disease Control, Atlanta, the Department of Medicine, Peter Bent Brigham Hospital and Harvard Medical School and the Harvard School of Public Health, Boston, and the John F. Kennedy School of Government, Cambridge, MA (address reprint requests to Dr. Koplan at the Office of Program Planning and Evaluation, Center for Disease Control, Atlanta, GA 30333).

**Vaccine Coverage (Points 2 and 3)**

Under the decision to have a vaccination program, chance point 2 divides the population into vaccinated and unvaccinated groups. We assumed that 90 per cent of the cohort would be vaccinated by six months of age, according to the level of vaccination for Massachusetts in 1977, the state from which we derived incidence figures. (This level may be considered a practical and desirable nationwide goal.) Furthermore, we assumed that all children vaccinated by six months would receive a booster dose at 18 months. We assumed that, without a vaccination program, none would be vaccinated (point 3).

**Vaccine Complications (Point 4)**

Pertussis-vaccine complications (point 4) can be grouped as "minor" and "major." Minor reactions include fever, soreness at the injection site, malaise and bodily aches lasting up to 48 hours after vaccination, and have been observed in one of 10 vaccinees on a three-dose schedule,[6,7] but a recent study has found a minor-reaction rate of two per 10 doses (eight per 10 vaccinees on a four-dose schedule [Hopkins RS: Epidemic Intelligence Service Conference, Atlanta, April, 1978]). We chose to use a minor-reaction rate of five per 10 vaccinees in a four-dose program. Major reactions consist of several types of neurologic irritation, which independent investigators have classified differently — e.g., some label a single convulsion as "seizures" whereas others view only repeated convulsions as a "seizure" reaction.

For this analysis we used estimates of rates of major reactions from two sources. First, the rate of moderately severe reactions, based on data from Sweden,[8] is one in 3100 vaccinees; these consist of convulsions (at least one), shock (sudden loss of consciousness with flaccidity and pallor or cyanosis, lasting up to 30 minutes), meningeal involvement ("abnormal cerebrospinal-fluid examination") and persistent, uncontrollable screaming (lasting more than 12 hours or requiring hospitalization). The rate of severe reactions is one in 34,000 vaccinees; these consist of repeated convulsions, hypsarrhythmia or serous meningitis, and the rate of encephalitis (not further defined) is one in 170,000. There were no data on the rate of residual defects or death in post-vaccination encephalitis; we therefore used the rates of residual defects and case fatality for the encephalitis associated with pertussis (see below). Secondly, unpublished and unofficial data from the Netherlands provide even higher estimates of vaccine-related major reactions (Hannik CA: personal communication, Rijks Instituut Voor de Volks Bezondheid, Bilthoven, The Netherlands, 1978). Shock occurred in one in 3500 vaccinees, convulsions ("at least one") in one in 2150 and persistent screaming ("unusual crying") in one in 3500. Over 20 per cent of children with shock and nearly 50 per cent with seizures had a family history of neurologic disorders. Febrile convulsions were considered "seizures." Encephalitis (undefined) was noted in four of 190,000 vaccinees; this rate is similar to an estimate of one in 54,000 in Scotland.[1] Accordingly, in the sensitivity analysis we used the following rates as the most pessimistic approximations of vaccine reactions: screaming, one in 3500; shock, one in 3500; convulsions, one in 2150; and encephalitis, one in 50,000.

The question of a possible association of DTP vaccination and sudden-infant-death syndrome was raised when a cluster of cases of the syndrome occurred recently in Tennessee. However, the association was not statistically significant in this occurrence.[9]

**Vaccine Efficacy (Points 5 and 6)**

On the basis of studies of intrafamilial secondary cases,[6,10] we considered that the vaccine would be effective in 70 per cent of vaccinees, and that 30 per cent would be left susceptible (points 5 and 6). Vaccine ef-

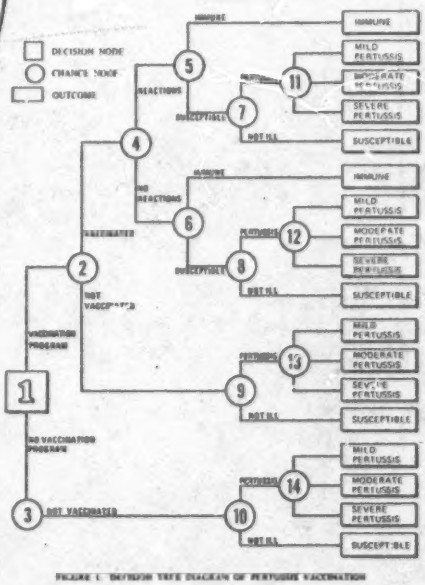


Figure 1. Decision Tree on Inclusion of Pertussis Vaccine in a Vaccination Program (See Text).

ficacy is inversely related to time elapsed since the previous vaccination, and can be estimated at 79 per cent for the three years following vaccination and 53 per cent for the next three.[10] The post-vaccination intervals for our study population ranged up to 4.5 years; 70 per cent average efficacy probably is a reasonable estimate.

**Pertussis Incidence (Points 7 through 10)**

Incidence rates in a population with a pertussis vaccination program were based on reports to the Massachusetts Department of Public Health for 1977. The rates (per 100,000 population per year) for susceptible children (points 7 through 9), under the assumptions of the model, would be 7.5 for those up to five months of age, 10.9 for those six to 11 months and 2.0 for those one to five years. We assumed that pertussis confers immunity for at least six years.

To estimate the incidence of pertussis in the absence of a vaccination program, we first determined the yearly incidence of pertussis in Massachusetts, where the disease has been reported since 1910 (Fig. 2), and assumed that the reported number of cases was a stable index of the true number throughout the 67-year period. Pertussis incidence declined in the period 1940-1950, before the widespread use of vaccine (state vaccination began in 1950); vaccine had been used to an undetermined extent by private practitioners for several years before. Since communicable diseases tend to decline exponentially, we therefore fitted pertussis incidence rates from 1940 to 1950 to a simple regression equation of the logarithm of incidence versus time, and extrapolated the regression line beyond 1950 to simulate what might have occurred if widespread immunization had not been introduced: in the absence of a vaccination program the predicted incidence rate for 1977 would have been 71 times the reported rate (point 10). If the incidence rates from 1920 to 1950 are used to determine the regression line, the predicted incidence rate for 1977 would have been over 600 times the reported rate. We also assumed that distribution of cases according to age in a population without a pertussis vaccination program would be the same as that observed before the introduction of pertussis vaccine in Massachusetts, when approximately 10 per cent of all cases occurred in each of the first six years of life.[11]

Figure 2. Observed Incidence Rate of Pertussis in Massachusetts, 1910 to 1977.
Regression line ($\log_e = -0.034878_x + 2.354635$) (dashed line) shows predicted incidence rate extrapolated from observed rates for 1940 through 1950.

Table 1. Severity of Cases of Pertussis According to Age.[12]

| Age | Per Cent of Cases | | |
|---|---|---|---|
| | Mild | Moderate | Severe |
| 0–5 mo | 0.40 | 0.39 | 0.21 |
| 6–11 mo | 0.75 | 0.16 | 0.09 |
| 1–5 yr | 0.95 | 0.033 | 0.017 |

**Severity and Complications of Pertussis (Points 11 through 14)**

We grouped cases of pertussis into three categories: mild (not requiring hospitalization but having an average of four weeks of illness), moderate (requiring hospitalization because of the severity of the disease but not having complications) and severe (requiring hospitalization due to complications — cyanosis, pneumonia, apnea, seizures and encephalitis). Severity varies with age[12] (Table 1).

The rates of complications in patients hospitalized have been estimated: pneumonia (20 per cent), apnea (5 per cent), seizures (5 per cent), death (1 per cent) and encephalitis (0.3 per cent).[13,14] In patients with encephalitis, the case-fatality rate is 33 per cent, and the rate of residual defects in survivors is 50 per cent.[15]

### ...al-Care Costs

...e tabulated the direct costs of pertussis and immunization according to the following assumptions. We assumed that a case of uncomplicated pertussis without hospitalization requires two physician visits at $11 per visit.[16] An in-hospital case (including various complications) requires an average stay of two weeks[15] at $175 per day[17] (including costs of such services as laboratory tests and consultants). Treatment for residual neurologic defects from pertussis encephalitis costs an average of $5000 per year, the defects persisting for a lifetime of 50 years. All future costs were discounted to present value at an annual rate of 5 per cent.

We also assumed that most minor vaccine complications are handled by telephone consultation or tolerated by the vaccinee and family without consultation. On the basis of a recent survey (Hopkins RS: Epidemic Intelligence Service Conference, Atlanta, April, 1978), 2 per cent of minor reactions require a physician visit at $11. Some reactions — a single seizure, shock or screaming — require two days of hospitalization at $175 per day; repeated seizures require seven days of hospitalization for diagnosis and treatment.

We further assumed that post-vaccination encephalitis requires a 14-day hospital stay at $175 per day. Treatment of residual defects of vaccine-associated ...phalitis costs $5000 per year for 50 years (costs w... discounted to present value at an annual rate of 5 per cent).

Pertussis vaccine in a DTP preparation costs approximately $0.076 more per dose than diphtheria-tetanus vaccine (Buchanan R: personal communication, Warner-Lambert Company, Ann Arbor, 1979); four doses cost $0.304 per vaccinee. There is no incremental cost for administration of pertussis vaccine because diphtheria and tetanus toxoids would probably be given at the same time in a vaccination program.

## Results

### Benefit-Risk Analysis

We predict a considerable increase in the number of pertussis cases and complications (Table 2) if pertussis vaccine is not included in community vaccination programs. However, vaccine reactions also contribute to morbidity and mortality in a program including this vaccine. We predict that with a vaccination program in a cohort of one million, there would occur five cases of post-vaccination encephalitis (Table 3, data from Sweden) and 0.1 case of pertussis-associated encephalitis (Table 2); without a program ... would be 2.3 cases of pertussis-associated en... alitis. We predict 0.3 death from pertussis and 1.7 deaths from post-vaccination encephalitis with a vaccination program as compared with 7.6 deaths from pertussis without a vaccination program.

Table 2. Predicted Cases and Complications of Pertussis, with and without a Vaccination Program, in a Cohort of One Million Children.

| | Cases | Complications | | | | | |
|---|---|---|---|---|---|---|---|
| | | Pneumonia | Apnea | Seizures | Deaths | Encephalitis | Residual Defects |
| With program* | 95 | 5.9 | 1.5 | 1.5 | 0.3 | 0.1 | 0.03 |
| Without program† | 6745 | 152 | 38 | 38 | 7.6 | 2.3 | 0.8 |

*Assumes 90% immunization coverage, 70% vaccine efficacy and incidence rates based on 1977 reported cases.

†Assumes no coverage and an incidence rate predicted from the trend of incidence during the 10 yr before routine program use of vaccine.

### Benefit-Cost Analysis

A comparison of the direct costs, with and without a community pertussis vaccination program (Table 4), shows that the program would reduce by 61 per cent the costs of pertussis — $720,862 versus $1,866,153 for each cohort of one million children (a benefit-cost ratio of 2.6:1).

### Sensitivity Analysis

We used the most pessimistic rates for all factors in this study, except for vaccine reactions for which we estimated the rate of minor reactions and then used the highest published rate of major reactions.

If unpublished rates of major vaccine reactions in the Netherlands were used in the analysis (Table 3), there would be 0.1 case of pertussis-associated encephalitis and 18 cases of post-vaccination encephalitis, with a vaccination program, as compared with 2.3 cases of pertussis-associated encephalitis, without a

Table 3. Rates and Predicted Cases of Major Reactions in Pertussis Vaccination Programs.*

| | Rate | Cases |
|---|---|---|
| Data from Sweden[4] | | |
| Convulsions, shock, meningeal involvement, screaming | 1/3100 | 290 |
| Repeated convulsions | 1/34,000 | 26 |
| Encephalitis | 1/170,000 | 5 |
| Data from the Netherlands | | |
| Convulsions | 1/2150 | 419 |
| Shock | 1/3500 | 257 |
| Screaming | 1/3500 | 257 |
| Encephalitis | 1/50,000 | 18 |

*Assumes 899,896 children in program — i.e., a cohort of 1 million minus both those acquiring pertussis during their 1st 6 mo and those ... vaccinated in a program with 90% immunization coverage.

Table 4. Comparison of Costs of Disease and Vaccine, with and without a Pertussis Vaccination Program.

| | Costs with Program ($)* | Costs without Program ($)† |
|---|---|---|
| Disease | | |
| Pertussis | | |
| Cases not hospitalized | 1,267 | 110,465 |
| Cases hospitalized | 68,189 | 1,682,664 |
| Encephalitis (residual defects) | 2,738 | 73,024 |
| Subtotal | 72,194 | |
| Vaccine | | |
| Cost of vaccine | 257,601 | |
| Reactions | | |
| Minor | 96,581 | |
| Repeated seizures‡ | 31,073 | |
| Screaming, shock, etc‡ | 99,024 | |
| Encephalitis | | |
| Hospitalization | 11,951 | |
| Residual defects | 152,438 | |
| Subtotal | 648,668 | |
| Total | 720,862 | 1,866,153 |

*Assumes 90% immunization coverage, 70% vaccine efficacy and incidence rates based on 1977 reported cases.

†Assumes no coverage and an incidence rate predicted from the trend of incidence during the 10 yr before routine program use of vaccine.

‡On basis of reaction rates in Sweden.[9]

program. There would be 0.3 death from pertussis and six deaths from post-vaccination encephalitis, with a program, as compared with 7.6 deaths from pertussis, without a program. The costs incurred from disease and vaccine in a program would be $1,226,060, as compared with $1,866,153 without a program. Thus, in this sensitivity analysis, the inclusion of a highly toxic pertussis vaccine, under a community program, would result in considerably more cases of encephalitis, a similar number of deaths and a saving of 34 per cent of costs, as compared with an immunization program without the vaccine.

The benefits of immunization are eliminated when the benefit-cost ratio is 1; this may happen when the rate of post-vaccination encephalitis reaches one case in 22,500 vaccinees, a rate almost eightfold higher than the highest published rate of one in 170,000.[9]

We assumed that the cost of care of residual defects from post-vaccination encephalitis averages $5000 per year for 50 years, discounted at 5 per cent per year. If the yearly costs are $10,000 and $20,000, the benefit-cost ratios are 2.2 and 1.8, respectively. The average cost would have to increase to $75,000 per year to reduce the benefit-cost ratio to 1.

In our analysis, which produced a benefit-cost ratio of 2.6, we assumed that a pediatric outpatient visit costs $11 and that hospitalization costs $175 per day (figures based on published national averages). If a pediatric visit costs $22, the benefit-cost ratio is 2.4; if hospitalization costs $350 per day, the ratio is 3.8. If all estimates for care that we used are doubled (pediatric visit, hospitalization, and care for defects left by post-vaccination encephalitis), the benefit-cost ratio is 3.2.

We extrapolated observed pertussis incidence rates and predicted that in the absence of a vaccination program a rate of 71 times the rate observed would occur. The predicted incidence rate, in the absence of a vaccination program whose benefit-cost ratio is 1, is between 23 and 24 times the observed rate, or about one third of the extrapolated rate used in our analysis.

## Discussion

This analysis provides a framework for examining the controversy over pertussis vaccine. It predicts different outcomes for the alternatives of having or of not having a community pertussis vaccination program. The cases of pertussis that would occur without a program, each accompanied by substantial morbidity, far outnumber the moderately severe vaccine reactions of shock, seizures and screaming that accompany a program. Cases of encephalitis, most postvaccinal, occur twice as frequently with a program, but deaths are almost four times as frequent in the absence of a program. Overall, the vaccination program should provide a saving of health-care resources. Under the assumptions and outcomes we have presented, there appears to be merit in continuing and promoting pertussis immunization.

Indirect costs of pertussis or immunization, not considered in our analysis, include future earnings lost because of permanent disability or premature death. We expect 3.7 cases of permanent disability or death with a vaccination program, and 8.4 without one. If indirect costs are included in the analysis, the net benefits of vaccination are increased. According to the vaccine reaction rates of the unpublished Dutch study there would be 12.3 cases of permanent disability or death with a vaccination program versus 8.4 cases of permanent disability or death without one. The net cost of lost earnings in 3.9 cases (estimated to be $45,000 per lifetime)[10] would decrease the net benefit of the program but still leave a saving of 30 per cent. Also, if the indirect costs of parental time spent caring for sick children were included, the total costs of not having a vaccination program would markedly increase.

Our analysis indicates that three factors are critical to the conclusions. The first is the frequency of occurrence of vaccine reactions. We used high estimates from Sweden and the Netherlands, where vaccine production and formulation are different from the United States. To the extent that the vaccine used in the United States might cause fewer reactions than the estimates we used or that a less toxic vaccine could be developed, a program of vaccination would look more attractive.

The second factor is the frequency of complications of disease. If the rates of respiratory or neurologic complications are higher than those we used, vaccination would be of even greater benefit.

The third is the extent to which pertussis and its complications would increase if immunization were discontinued. In the United Kingdom, controversy about pertussis vaccination over the past few years has led to a considerable decrease in immunization of newborns. A 10-fold to 16-fold increase in pertussis cases has been reported from some regions of the country, and is leading to recommendations that immunization be reinstituted vigorously.[19]

Some lag after initiating a program should be expected before full benefits are achieved. As cohorts immunized in childhood age, their immunity may help to limit spread to younger children; protection is not complete, however, as shown by recent outbreaks among immunized adults.[20,21] The lag in realization of benefits may explain in part the continuing divergence between the observed and the predicted incidences of pertussis in Massachusetts (Fig. 2). Also contributing to the divergence is the steadily increasing proportion of children immunized in the state.

It should be reemphasized that our assumptions and the data on which they are based are taken from conditions and studies in the United States and Western Europe. In developing countries, pertussis and its complications are of much greater incidence and severity.[22] The level and distribution of clinical cases associated with a low case-fatality rate in more developed nations are often not found in less developed parts of the world, where case-fatality rates of 1.2 per cent have been reported.[22] Therefore, with considerably increased risks from pertussis and probably similar risks from pertussis vaccine, the net benefits of vaccination should be far greater for developing nations than the benefits estimated for the United States and Western Europe.

The subject of pertussis vaccination has prompted debate and letters to medical journals. These responses in turn have led to decreased public acceptance of pertussis vaccine in some countries. Our analysis of pertussis vaccination programs demonstrates that the benefits of vaccination outweigh the risks, and that the savings outweigh the costs. If one considers only the worst possible situation, by using the highest estimates of reaction rates, the results are less clear-cut. Our analysis supports the continuation of pertussis vaccination in routine childhood immunization programs, but suggests the need for prospective collection of reliable data on vaccine complications in a large population, close observation of the epidemiology of pertussis in the United Kingdom and the United States, and development of a less toxic vaccine.

We are indebted to Dr. Nicholas Fiumara for information on reported cases of pertussis in Massachusetts and to Mr. Norman Staehling, Mr. Paul Strange and Dr. Andrew Sumner for assistance.

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Dr. PARROTT. This used available data—some have been referred to earlier—including some of the worst estimates of pertussis vaccine induced frequency of encephalitis, and then the study projected the potential frequency of certain complications of an immunization program versus abandoning such a program. And estimates are then given for certain events occurring per million children, and the figures—I will give you just some of them. If the immunization program continues, there would be 95 cases per million children of pertussis. If it is stopped in this country, there would be 6,745 cases of pertussis; of pneumonia, 5.9 per million, if the program continues, and 152 per million if the program is eliminated.

In general, there are about 25 times more of each event that is listed—apnea, seizures, death, encephalitis, or residuals—if the program is eliminated than if it is continued.

The conclusion of that article is that the "analysis of pertussis vaccination programs demonstrates that the benefits outweigh the risks and that the savings outweigh the costs." The analysis supported the continuation of pertussis vaccine in routine childhood immunization, did support the prospective collection of reliable data on vaccine complications in a large population, continued close observation of data from other countries such as the United Kingdom, and the development of a less toxic vaccine.

And I would state indeed, it would be desirable to have a less toxic vaccine, and we all support continued research toward that goal. Meanwhile, we advocate continued use of the pertussis vaccine and routine immunization and continued discussion of the issues and sharing information on the potential risks, particularly with health workers, so they can interpret them to families when indicated.

Also, one would have to insist on adherence to criteria which will minimize the likelihood of serious reaction. And, rather than reading through them, I will just indicate there are certain agreed upon precautions and contraindications. Essentially, however, they can be detected only after one has occurred. There is no really good way of knowing in advance which child might be at risk of these complications. So the precautions and contraindications as listed by the Public Health Service Advisory Committee on Immunization Practice or by the Red Book Committee are essentially the same. They include certain conditions that would say if one sees it, then do not reimmunize; collapse or shock, persistent screaming, high temperature, convulsions with or without fever, severe alterations of consciousness, generalized and/or focal neurologic signs, systemic allergic reactions, a drop in a certain blood cell, or hemolytic anemia,

I will not read through the others. The other point is that pertussis component is not recommended for use after the age of 7, essentially because it is more likely to be reactogenic after that, and the danger of death is less after that.

I believe a related issue is the potential of a program of compensation from the Government for vaccine-related injuries. In the rare instance where a neurologic complication apparently occurs, the family can undergo considerable financial burden, and in despair, as has already been indicated in a recent panel, the only thing they can do is sue the physician or manufacturer for liability.

The physician is equally as disturbed as the parents when such a reaction occurs, and is set into a circumstance where in fact, when he may within his heart, want such compensation to occur, he has to defend his own and his family's future financial security.

So I believe a workmen's compensation-like recompense would be much more just and appropriate to the situation.

Thank you, Senator.

Senator HAWKINS. Thank you, Dr. Parrott.

What questions should a parent ask a physician before his or her child receives the vaccination, in your opinion?

Dr. PARROTT. Well, one would hope that there is a realtionship with the pediatrician or the clinic wherein the potential risks had been raised, and I think, however, an intelligent parent, one who reads general literature on child raising, will know that there may be certain reactions, so that in general, as time goes on and as parents are more informed and there is more of a consumer advocacy sense in the country, I think it is reasonable for them to asks, "Well, are there some risks, and how do these measure up against the benefits?"

Senator HAWKINS. You have heard the testimony this morning of parents who stated that the doctor says to brings their children in on the third of the month, and we will give them their DPT shot, and they really had no idea whatsoever of any possible reaction.

Dr. PARROTT. Right. I cannot controvert that testimony specifically in those particular cases and also cannot necessarily condone what occurred. However, in my opinion we are in a time of change with occurred. However, in my opinion we are in a time of change with respect to how patients and families and doctors and the health system interreact. I think it is true that in the past, families wanted physicians, nurses, and so forth to be the authority, to say, "This is what you should do." I think now, with an increased education of the population and with a consumer advocate attitude, that both medicine will have to change, and apparently, the public is changing. So that increasingly, physicians and health systems will do things in ways that were not done before. Will share more in certain decisions.

I have done an iformal survey of privately practicing prediatricians, and as far as I can tell in this area, or at symposia where I may have been participating on a national basis, about one-third only of individually practicing pediatricians use a piece of paper, a permission form, an informed—if it is informed—consent. About two-thirds in some way discuss the potential risk, and some in great detail, with the family. That would mean that about one third do not routinely do much discussing with the family. They are those who are of view that the family wants them to be the authority, to tell them what to do, to weigh the risks and benefits. I think that times may be changing in respect to these matters.

Senator HAWKINS. Is it possible to test children to determine their natural immunity before they are vaccinated?

Dr. PARROTT. Technically, it would be possible, but it would be impractical. The tests exist. They are similar to the ones that are done with mice. But one does not gain significant antibodies from the mother. Therefore, it is in general known that there is very little transplancental antibody or protection from the mother, and

that the newborn baby is at risk, so there is not much point in testing.

The only potential value would be in an older individual who might be entering a helath system and might be exposed, and maybe if would be good to know what the antibody levels were in that person, for the person to decide whether or not to have a booster, at a time when we usually do not give boosters. It is not parctical, Senator.

[The prepared statement of Dr. Parrott follows:]

Statement on Continued Use of Pertussis Vaccine

by Robert H. Parrott, M.D., Director

Children's Hospital National Medical Center

An NBC television program of April 20 raised questions about use of the pertussis or whooping cough component of "routine childhood immunization". The coverage gave heavy and emotional emphasis to possible neurologic reactions of the vaccine. It was suggested that physicians were not aware of or were not disclosing to families the potential risks.

In fact, public health and pediatric leadership in the country have carefully reviewed the potential risks versus the benefits of the pertussis vaccine and concluded that routine immunization should be continued. Also, many feel that over-emphasis on the risks might lead to a situation such as has occurred in sections of Great Britain where "more children died (of pertussis) in the 1977-79 epidemic than would at the latest risk estimates have been severely damaged by vaccination." (Lancet, May 23, 1981, page 1139). The current view of the British government is "that the balance of risks is in favor of continued vaccination with stringent attention to contraindications."

One of the problems in our country is that whooping cough vaccine use has been so effective that young families and young health workers are not familiar with the disease. Perhaps somehow we need to turn back the clock to the 1920's or 30's when 100,000 to 250,000 cases were reported a year. Perhaps we need more testimony from grandparents who remember. There is a catarrhal or cold-like stage with symptoms of a cold, sneezing, watery eyes, cough and low grade fever. During this stage when the responsible germ is growing and multiplying at the greatest rate and when an individual can spread the germ, whooping cough is not suspected. There is then a

paroxysmal or whooping stage. Let me just read a description of the disease from one of the standard textbooks: "The cough now comes in explosive bursts; a series of 5 to 10 or more short, rapid coughs is given on one expiration and is followed by a sudden inspiration associated with a characteristic high-pitched crowing sound or whooping.....The child's face becomes red or blue, the eyes bulge, tongue protrudes and the whole expression is anxious or utterly miserable. A number of these attacks may be grouped together until the child succeeds in dislodging a plug of mucous. Vomiting frequently follows. Then the child often appears listless, dazed or out of touch.....is likely to sweat profusely and show swelling of the face. During the first one or two weeks of this stage the attacks increase in severity. They continue for one to three weeks. Then there is a convalescent phase and some children will develop recurrent coughing attacks complete with the whoop and vomiting after other infections for one or two years." "The most common, and usually the most severe complication is pneumonia, especially feared in infants under one year of age. This can lead to chronic lung problems with sacs of pus (bronchiectasis), collapse of the lung (atelectasis) or air trapping (emphysema). This latter is a common postmortem finding and probably exists in the lungs of many patients. Convulsions may result from the loss of oxygen during severe paroxysms and from small bleeding spots in the brain. Bleeding can occur in the eyes, nose, skin as well as the brain. The tongue may be injured in the cough. The fatality rate is less than 10 per 100,000 cases and most deaths occurred in infants."

"The severity of pertussis is not commonly appreciated. The greatest danger from it occurs in infancy. When the outlook for an individual

patient is assessed, the presence of complications has an important bearing on his future health as well as on his immediate survival. Interstitial pneumonia that is unresolved or slow to resolve and persistent atelectasis are common danger signals of bronchiectasis. The onset of asthma has been observed to follow whooping cough. Cerebral manifestations are ominous. Sudden death from asphyxia due to obstruction of the airway may occur in uncomplicated cases. This emphasizes the vital importance of close nursing supervision."

A recent analysis of the risks and benefits of pertussis vaccine (NEJM Vol. 301, page 908, 1979) used available data, including some of the worst estimates of pertussis vaccine-induced frequency of encephalitis, to project the potential frequency of certain complications of an immunization program versus abandonment of such program.

Complications of Pertussis in 1 Million Children

| | Immunization Program | |
|---|---|---|
| | Existing | Eliminated |
| Cases | 95 | 6745 |
| Pneumonia | 5.9 | 152 |
| Apnea | 1.5 | 38 |
| Seizures | 1.5 | 38 |
| Deaths | 0.3 | 7.6 |
| Encephalitis | 0.1 | 2.3 |
| Residuals | 0.03 | 0.8 |

The conclusion of this article is quoted:

"Our analysis of pertussis vaccination programs demonstrates that the benefits of vaccination outweigh the risks, and that the savings outweigh the costs....Our analysis supports the continuation of pertussis vaccination in routine childhood immunization programs....prospective collection of reliable data on vaccine complications in a large population, close observation of the epidemiology of pertussis in the United Kingdom and the United States, and development of a less toxic vaccine."

Indeed it would be desirable to have a less toxic vaccine and we all support continued research toward that goal.

Meanwhile, we advocate continued use of pertussis vaccine in routine immunization of infants and continued discussion of the issues and sharing information on the potential risks particularly with health workers so that they can interpret them to families when indicated.

Adherence to the following criteria will minimize the likelihood of serious reactions:

PRECAUTIONS AND CONTRAINDICATIONS (MMWR:30, 392, 1980)

1. When an infant or child returns for the next dose in a series of DTP injections, the parent should be questioned about severe side effects or adverse reactions after the previous dose. If any of the following occurred, additional doses of pertussis antigen are contraindicated, and immunization should be completed with DT: collapse or shock, persistent screaming episodes, temperature above 40.5 C, convulsion(s) with or without accompanying fever, severe alterations or consciousness, generalized and/or focal neurologic signs, systemic allergic reactions, thrombocytopenia, or hemolytic anemia. Lesser reactions than these do not, in themselves, preclude the further use of DTP.
2. The presence of an evolving neurologic disorder contraindicates use of pertussis vaccine. A family history of neurologic disease or a static neurologic condition like cerebral palsy is not a contraindication to giving vaccines containing pertussis antigen.
3. Ordinarily the pertussis component should not be used in individuals 7 years of age or over.

A related issue is the potential of a program of compensation from the government for vaccine-related injuries. In the rare instance where a neurological complication apparently occurs, the family can undergo considerable financial burden and in despair sue the physician or manufacturer for liability. A "Workman's Compensation-like" recompense would be more just and appropriate to the situation.

Senator HAWKINS. Thank you so much, Dr. Parrott, for the advice you hve given to us and to parents regarding immunization.

Dr. Fulginiti, I understand you hve a statement you would like to summarize for us.

Dr. FULGINITI. Yes. I have submitted, Senator Hawkins, a much more detailed document to you, but I will just read some briefer remarks, if I might.

Senator HAWKINS. Yes, we would appreciate it.

Dr. FULGINITI. Thank you very much for having me here. I am a pediatrician, I am a professor and head of the department of pediatrices at the University of Arizona in Tucson, and I also head the Committee on INfectious Diseases of the Academy of Pediatrics. Tthose are my reasons for being here.

.Our primary concern at the academy has always been and will continue to be the welfare of children, and one manifestation of this is that we have a series of committees whose function is to utilize voluntary participation by physicians across the country—all pediatricians—to consider data in their area of expertise such as nutrition, genetics—in our case, infectious desease and immunization—and then we present that as advice and guidelines to pediatricians in the form of the Red Books. (Report of the Committee on Infectious Diseases, 19th edition, 1982, AAP)

In contrast to what you heard earlier, my wife wishes we meet every 2 years. On a voluntary basis, we meet two to four times a year. We have conference calls anywhere from five to six times a year and my phone rings constantly, as chairman of the committee, from other members of the committee, from doctors all over the country, and from some patients. This is an activity that is ongoing, it is vital, it is dynamic. It is not something that we just do casually every couple of years.

As you pointed out in your opening remarks, children in the United States enjoy substantial freedom from the ravages of once common communicable infectious diseases and illnesses. These illnesses limited life expectancy and left tens of thousands disabled in their wake. We constantly forget this, because young parents today do not see these diseases, and so the obvious question is, "Why should I give my child vaccine?"

Smallpox has been eradicated in the world. There is no more smallpox. That is a remarkable accomplishment. Measles promises to be eradicated, as you heard earlier, in this decade, and whooping cough, rubella, mumps, diphtheria, and tetanus have been reduced to the lowest levels in our recorded history.

Although improved living conditions, better nutrition, and improved medical care partially contributed to this decline, the major reason for the sharp and deep reduction in these diseases, and in one case eradication, is directly attributable to the development and employment of effective vaccines.

Investigators, industry, the Federal, State, and local governments, and the private medical system in this country, have all contributed to this remarkable record of public health. In the lengthier document I referred to earlier, I have enumerated the ways in which each of these sectors have contributed, but in the light of your letter to me, I will only elaborate on the Federal component.

Federal funding for purchase of vaccines to be distributed to needy children has been a critical element in the entire system of immunizations. The establishment of standards for purity, potency, and efficacy of vaccine products, largely through the efforts of the Bureau of Biologics and the FDA, obviously is a very important function within the Government and should be supported, and the establishment of policy guidelines and advice for the use of the vaccines, largely through the efforts of the Centers for Disease Control, separately and in cooperation with the private sector such as our committee, are the three major functions of the Federal Government.

Despite the obvious success of vaccine development and deployment, problems still remain and certain threats to successful pursuit of vaccine use and reduction in disease have arisen in the recent past. These include: One, diminished Federal funding for vaccine purchase and for agencies and programs supporting immunization. We keep throwing figures around about how many millions of children are going to be vaccinated. There was a report in our local paper just before I left that 80,000 children in Phoenix next year will be unable to receive vaccine as a result of Federal cuts in the Vaccine Assistance Act. I like to think of these children as Mary and John and Joe and Jose. They are the ones who are not getting the vaccine, and they are the ones, then, who will be subject to these diseases, rather than trying to consider these numbers in the millions.

The second threat are legal suits against physicians, manufacturers, public health agencies, and advisory bodies for alleged and actual injury resulting from vaccine administration.

And the third threat is unwarranted, unbalanced, focus by the media in sensationalistic fashion upon the problems of immunization without a counterbalanced consideration of the vastly outweighing benefits.

Now, the toll caused by injuries secondary to vaccine use can only be compensated in this country by successful pursuit of redress under the tort laws, often resulting in anguishing trials for both plaintiff and defendant, and I pity both parties in a trial of this type, as Dr. Parrott said.

Decisions in the legal arena are often made emotionally and without regard to the facts in the specific case. The Academy of Pediatrics has long favored a vaccine compensation system and is actively promoting this concept, along with Mrs. Betty Bumpers, with various branches of the Federal Government, with the view that a national system would be established to compensate fairly all persons injured as a result of the remote intrinsic risks associated with all vaccines. We firmly believe that this system should be set up, and have pushed for this for a number of years now.

Finally, reporters, local TV and radio stations, networks, and print media tend to focus on the risk side of the equation of benefits and risks from vaccines. The most recent and outstanding example is the NBC program, "DPT: Vaccine Roulette," aired locally by WRC-TV in the Washington area on April 19 and excerpted for presentation on the national "Today" show on April 20. In the wake of these two programs, many thousands of concerned and unnecessarily frightened citizens contacted their physicians express-

ing alarm, dismay, and in many cases, hostility. The program had numerous flaws, some of which I have detailed in the lengthier document presented to you. Basically, the examples I have included illustrate unbalanced reporting with dramatic emphasis on the negative; bias, evident from the frivolous title, "Vaccine Roulette," of the program, and in the editing and statements made on the show; and inaccuracies in the "facts" presented.

The impact is serious. Many parents are refusing immunization, with pertussis vaccine and with all vaccines. Some physicians in the intensity of the focus on this issue have decided to drop pertussis vaccine. One pediatrician in my community suggested that what he might do is to send all of his children down to the public health department and let them give the vaccines, so he would be out of the "craziness" as he referred to the current frighted response of parents.

These events are regrettable, if one keeps in mind that England had a similar sequence in the late 1970's, which resulted from media over-attention to alleged risks of pertussis vaccine. Immunization rates dropped from 79 percent in 1974 to 31 percent in 1978. In contrast to what was said on the show, beginning in 1977 and extending through 1980, 102,500 cases of pertussis occurred; 28 children died; and 5,000 were admitted to hospitals. And 200 of these children had convulsions.

Similarly, in Sweden, on the show, a map was shown with Sweden and West Germany depicted as having dropped pertussis vaccine. West Germany does not report pertussis, so we have no idea what the experience is there. Private reports indicate an epidemic in 1979 and another this year. But in Sweden, since 1978, when that country dropped its own vaccine that it made because of lack of potency, 8,000 cases of pertussis have occurred. That seems like a small number, but there are only 8 million people in Sweden, less than in the city of New York, and that gives a case rate of 100 cases per 100,000, or 1 in 1,000. That rate is comparable to other countries in the Western World, before pertussis vaccine was ever used.

The major point of all this is that pertussis is a crippling disease. The Chinese have an ideogram for pertussis, and the ideogram is translatable, literally, as "hundred-day cough." They recognize that this is a long disease and a very complicated disease. Children with this illness cough unmercifully. It is almost impossible for any sense to be given to someone who has not seen the disease. They choke in the process. They gasp for air. They often vomit, become dehydrated and acutely undernourished. They may destroy parts of their lungs and brain from hemorrhage and anoxia, lack of oxygen.

Furthermore, it is often complicated by chronic disability and death, as you have heard. Now, these complications have been largely eliminated in the United States by widespread use of a highly effective vaccine. The vaccine is not perfect. It does have a number of transient, nonpermanent side effects, but only rarely produces serious adverse effects. And even more rarely does it cause permanent damage or death.

I do not wish to add to the mother's grief who testified earlier, because I have great sympathy for her and her child and the long period of troubles that they have had. But infantile myoclonic sei-

zures have been studied very carefully and are not ordinarily attributable to any event that we know, including pertussis vaccine. In fact, there is a large scale study showing that infantile myoclonic seizures occurred in a country where no pertussis vaccine was given, at the same frequency and in the same age group. So it is possible that the reason there was a 2- or 3-week interval from the vaccine to the onset of that disease is that the two were not connected at all.

The various governmental agencies and advisory professional groups, such as the American Academy of Pediatrics and the Centers for Disease Control, have been knowledgeable about all the benefits and risks from both the disease and the vaccine and have responsibly transmitted this information to physicians in diverse and effective ways. There has been no conspiracy to conceal facts, as hinted at and implied on the TV show, nor has there been any attempt to minimize or hide adverse reactions on anyone's part.

I have been an outspoken advocate of weighing the risks of vaccine against the benefits of vaccine and the risks of disease, for a long period of time now. I can assure you that each of the advisory bodies—and I have sat on these committees for 7 years, now—very seriously weigh benefit/risk. As you heard earlier, we eliminated smallpox vaccine when in this country it became apparent that the risk from the vaccine exceeded the risk from the disease. We have no hesitation in eliminating a vaccine if that is the case. However, for all currently used vaccines including pertussis vaccine, the benefit/risk ratio is clearly in favor of the vaccine, and none of the vaccines should be stopped.

Now, efforts continue in governmental, manufacturers' and investigators' laboratories to better understand the bacterium that causes pertussis, the body's response to it, and ways to make an equally or even more effective vaccine, which has few or no side effects. This is not an easy task. The same chemical principles in the bacterium that produce the immune response in the host also have toxic properties, and it has been very, very difficult to separate those two elements and insure that the child is going to be protected and yet have no side effects. And that is what has hampered the efforts—not because anybody has been reluctant to do it, or there has been no interest. We simply have had difficulty separating those two effects of the bacterium.

Pediatricians and other physicians and health care workers caring for children have as their primary concern the well-being and welfare of their patients. In using pertussis vaccine, they are exercising the best available scientific judgment, which clearly establishes that the vaccine prevents a major debilitating disease but is balanced by some risk. Everything we do for patients carries a risk, and we consider it in the same light—a balance between the risks of what we do against the risks if we do nothing.

If I prescribe an antihistamine for a child who has hay fever, if I prescribe penicillin for a child who has a strep throat, or if I prescribe pertussis vaccine to prevent whooping cough, the advice I am giving the patient is, this treatment has less risk than the disease which we are either trying to treat or prevent. Penicillin can kill, itself, but so can a strep throat, and the balance between the two is clearly in favor of giving penicillin. The same thing is true of pertussis vaccine.

I consented that pertussis vaccine be given to all four of my children. I advise my patients to receive it. I teach my students and residents about it and recommend its use to them. And, as a member of the Committee on Infectious Diseases of the American Academy, I continue to advise all physicians in this country to use pertussis vaccine.

The NBC show tended to undermine this balanced judgment, relied upon an imbalanced view—bias, in my view—and inaccuracies to carry its destructive message. In my view, this program was not an example of responsible journalism.

In conclusion, immunization has been an effective medical and public health tool and has reduced or eliminated infectious diseases which once were the scourge of childhood. This effect has resulted from a cooperative effort between government, industry, and the private sector. Our efforts today are threatened by decreased governmental expenditures for vaccine and other programs, by an unwieldy legal system, and by unfair sensationalization by the media of only one part of the total vaccine benefit/risk equation. We should and must counter each of these threats to continue to ensure our youth a healthy childhood.

Thank you.

Senator HAWKINS. Thank you. I share the Academy's concern and your private concern that fewer children will be immunized unless more Federal money is provided to the States. At the same time you state that you have been receiving a lot of telephone calls from pediatricians who are upset since the television show dramatized the adverse reaction situation. Is there any conversation in the Academy or among your associates to encourage private physicians to adequately inform patients and parents of the warning signs that may indicate that the child is experiencing a reaction?

Dr. FULGINITI. Yes. Like Dr. Parrott, I have had the experience of talking around the country. In the last 2 meetings, which together covered more than 500 pediatricians, about two-thirds of the pediatricians are using some form of informed consent, either the important information documents, or verbal communication to their parents, or a sign on the wall with all of the vaccines, listing all of the complications, or their own documents—in one case, the pediatrician completely wrote his own document out. The remainder are not using anything under the premise that "The patient comes to me for my advice, and I give him my best judgment."

In fact, in 2 years of using the informed consent forms in our own institution, 90 percent of the patients read the form and say, "Doc, what do you think?" and then do whatever we suggest.

Senator HAWKINS. Does the informed consent that private physicians use list the reactions to watch for?

Dr. FULGINITI. Yes; and what to do about them if they occur. The private physician usually also has an instruction sheet that goes along with it. That has changed, as Dr. Parrott said, from years past. The Red Book, which will be published very soon, as the latest edition of this advice, will strongly urge all pediatricians to give such information to their parents.

[The prepared statement of Dr. Fulginiti follows:]

# American Academy of Pediatrics

TESTIMONY

on

IMMUNIZATION PROGRAMS

before the

United States Senate
Subcommittee on Investigations and General Oversight
Committee on Labor and Human Resources

Presented by

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May 7, 1982

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Children in the United States enjoy substantial freedom from the ravages of once common communicable infectious diseases that limited life expectancy and left tens of thousands disabled in their wake. Smallpox has been eradicated worldwide, measles promises to be eradicated in this decade, and pertussis, rubella, mumps, diphtheria and tetanus have been reduced to the lowest levels in recorded history. Although improved living conditions, better nutrition and improved medical care partially contributed to the decline, the major reason for the sharp, deep reduction and, in one case, eradication of these diseases is development of effective vaccines. Many segments of our society have contributed:

1. Investigators in government, in private industry, in universities and in private practice have provided us with increased knowledge of the causes and mechanisms of these illnesses and with effective vaccines to prevent them.

2. Industry has responded with technological and marketing skills to make large quantities of vaccine available in usable form.

3. Governmental agencies have helped by insuring standards for vaccine production, by insisting upon purity and safety and providing advice and guidance to those using vaccines. In addition, the total governmental apparatus -- federal, state and local -- has provided funds, personnel and programs to administer vaccines to groups of children who utilize the public health system of care. And, finally, the Food and Drug Administration and Centers for Disease Control have worked with the private sector to develop national policies, to publicize need for vaccines, to develop methods for informing patients as to the risks of diseases and the benefits and risks of vaccines, and to establish models for use in individual health personnel/patient contacts, such as the Important Information documents developed by the CDC and now in wide use in both the public and private medical sectors.

4. Private Sector - By diligent use of vaccines as part of comprehensive well-child care, individual physicians have ensured that we have a well protected population. The American Academy of Pediatrics is proud of its contribution to these efforts in informing physicians about vaccines as they were developed, in providing guidelines for their use, and in establishing policies designed to inform patients of benefits and risks. The Academy has always placed the welfare of children as its highest priority and the vaccine effort reflects this commitment.

Currently there are a number of threats to this effective system for control of these diseases. Among them are: 1) reduction in federal funding for the purchase of vaccine for use by state health departments and others, 2) legal suits against physicians, health departments,

recommending authorities, and manufacturers for injury from vaccines, 3) sensationalism of reports of damage secondary to vaccine presented by the media in such a way as to discredit governmental agencies and physicians, to imply conspiracy, mal-intent or self-interest as a motivation among vaccine supporters, and to simplify complex decisions and judgments in vaccine policy.

Federal support for the Childhood Immunization Program is not only at one with HHS Secretary Richard Schweiker's avowed emphasis on prevention, it remains manifestly in the public interest. If the President's proposed funding level of $28.8 million holds sway during fiscal 1983 for the Childhood Immunization Program, vaccine delivery to children would be reduced to intolerably low levels. The 7 percent cut in the program imposed this year already has caused a 32 percent drop in vaccine purchases; meanwhile, the cost of vaccine has increased by 44 percent during the past two years. As a result, 33 percent fewer children are being served. An appropriation for fiscal 1983 of $32 million is essential if programs are to be maintained at their current levels. To allocate less flies in the face of compelling documentation that indicates an inverse relationship between federal support for vaccine programs and the incidence of diseases.

Our society simply cannot afford, morally or economically, to turn its back on the 3.5 million children born here each year. Based on past experience, these cuts proposed by the Administration would prove terribly costly and cruel -- costly in direct dollar terms to all of our citizens for many years to come, and cruel to the unfortunate victims and their families for a lifetime. No one can quantify the pain associated with these illnesses. Deafness, blindness, cerebral palsy, retardation and severe emotional disturbance can destroy children and their families. When the capacity to prevent these conditions is at hand, failure to protect our citizens is doubly cruel.

The toll caused by injuries secondary to vaccine use can only be compensated in this country by successful pursuit of redress under the tort laws, often resulting in anguishing trials for both plaintiff and defendant. Decisions in the legal arena are often made emotionally and do not necessarily follow the facts in a particular case. The American Academy of Pediatrics has long favored a Vaccine Compensation System and is actively promoting this concept with various branches of the federal government with the view that a national system should be established to compensate fairly all persons injured as a result of the remote, intrinsic risks associated with all vaccines through no fault of the physician or the manufacturer.

Physicians have been cognizant of the need for patients and their parents to be aware of the hazards of these diseases in children of the desirability of protection against them and of the balance between benefits and risks of the vaccines used in prevention. Each vaccine used has some risks associated with it. In developing vaccine recommendations and policy, the American Academy of Pediatrics, as well as the CDC, has advised physicians and other health personnel to inform patients and parents of the benefits and risks of vaccines.

The final threat is that which occurs because of sensationalized media accounts of vaccine side-effects. In England this type of imbalanced account of pertussis vaccine "dangers" results in loss of public confidence and an ensuing series of epidemics of whooping cough involving 102,500 children and 28 deaths. The United States is in potential danger from a similar sensationalized assault. Because of the terribly important implications for children's health, we at the American Academy of Pediatrics believe it imperative that such sensationalism not go unchallenged. For this reason I would like to detail the implications and impact of a recent major network program on disease control efforts.

The program's title, "DPT: Vaccine Roulette," the editing of interviews and statements made by the reporter and others exemplified 1) the program's imbalance as to the risks of pertussis (whooping cough) and benefits and risks of pertussis vaccine; 2) superficiality in the presentation of complex issues; and 3) biased and inaccurate statements. The importance of this negative report is in the large amount of attention given it by the media, concerned and unneeessarily frightened lay persons and physicians and health agencies.

Specific examples from the program include:

- An opening stating that "...DPT shot can also damage to a devastating degree." The fact is that serious, permanent residual of the brain damage type is rare following DPT -- once in 310,000 doses (100,000 children). The use of the phrase, "a devastating degree" is inaccurate since pertussis can cause brain damage in as many as one child in 8,000.

- The listing of "learning disabilities," unspecified, as caused by DPT vaccine. I know of no evidence linking learning disability as an isolated condition to DPT. Of course, if a child develops encephalopathy, one part of the possible residual from that might be a learning disbility. This is also an example of simplistic treatment of a complex area.

- The statement that "This is for sure, the Whooping Cough, or Pertussis, vaccine is the most unstable, least reliable vaccine we give our children." This is inaccurate; pertussis vaccine reliably protects about 80 percent of recipients of a full series from the disease, and even if the disease occurs in a vaccinated child it tends to be mild. I don't know what is meant by "unstable," because pertussis vaccine is stable; yet another inaccuracy.

- The statement that "The statistics of this country are wrong, and the danger is far greater than any doctors here have been willing to admit." This is a biased, untrue statement. Which "statistics" are wrong? Which doctors have been unwilling to admit? Reports of the Academy's Committee on Infectious Diseases and from the CDC have detailed the expected side effects and adverse reactions, as have a multitude of textbooks and scientific articles. There has been no reluctance displayed to widely

disseminate information concerning reactions as they were discovered. The effect of this excerpted comment is to imply wrongdoing -- there is absolutely no evidence for this and much to the contrary.

- It was stated that the currently used vaccine would not be produced today if it were just being introduced. However, there is no effective, proved alternative even with today's methodology. Pertussis vaccine may not be ideal, but it is effective and on balance far safer than having the disease.

- It was stated that "... in the 1930's whooping cough struck over 195,000 people and 4,800 died from the disease annually." In fact, as many as 265,000 people were reported to have the disease and 7,000 were reported to die annually. In a free society we depend on voluntary reporting which underestimates the actual occurrence; thus it is almost certain that many more people got pertussis and more than reported died annually.

  While it was stated that pertussis began to decline prior to use of vaccine, in Massachusetts, where accurate figures were kept, pertussis hovered around the 100-300 cases/100,000 by 1970 only after vaccine was introduced.

- It was stated that because of antibiotics, death from pertussis is a relatively rare event, yet of 1,000-3,000 cases reported annually 5-20 die. Our best estimates today are that the death rate in children hospitalized for pertussis is slightly less than one percent and higher in infants under six months of age -- hardly a relatively rare event.

- It was implied that in the post-discontinuation of pertussis immunization in England the epidemics that occurred were less than "U.S. officials" quoted: 66,000 cases and 12 deaths in 1978 and 21,200 cases and six deaths in 1980 were the figures cited as correct in the broadcast. In fact, the purportedly official United Kingdom sources that were quoted give the following figures:

  a. Immunization rates fell from 79 percent in 1973 to 31 percent in 1978
  b. 102,500 cases of pertussis from 1977-1980
  c. 28 deaths
  d. illness often protracted lasting 10-12 weeks
  e. 5,000 hospital admissions
  f. 200 cases of pneumonia
  g. 83 cases of convulsions

  It would appear that the U.S. "officials" are correct in their reporting. Further, the English "official sources" also pointed out that in children over five years of age (having been born during widespread use of pertussis vaccine) the attack rate of pertussis was 20-25 percent of the rate in children under five and

districts with lowest vaccine use had the highest rates of disease. They concluded that this is proof of vaccine efficacy and that the epidemic occurred because of the decrease in vaccine usage.

It was stated that serious reactions from pertussis vaccine "could be as low as one in every 700 children." The term serious is not defined but rather equated with brain damage and death. The truth is:

a. Transient, non-permanent side effects such as a lump, redness or a sore injection site are common, as is fever -- from 20-50 percent in most studies. These do not result in death, permanent disability or brain damage.

b. Drs. Cody, Baraff and Cherry, in the UCLA study referred to in the program, examined children's reactions after 15,752 doses of DPT and other children after 784 doses of DT. They found:

- 9 convulsions in 15,752 doses, a rate of 1:1750 or 0.057 percent. None of these children was abnormal on examination.

- 9 episodes of collapse -- the same rate -- all recovered without observable sequelae.

- 3.1 percent of persistent crying (more than one hour) but only 1:1000 children (0.1 percent) whose cry was high pitched and unusual.

c. Other estimates and measurements of convulsions include:

1:13,000 London study, 1975-1977
1:7,000 based on reports to CDC
1:3,200-1:50,000 Dr. Geoffrey Edsall
1:2,500 British study, 1948-1951
1:3,945 British study, 1956
1:2,666 British study, 1953-1957
1:6,453 Dr. Justus Strom, Sweden

Conclusion:

"Serious" reactions, defined as convulsions or collapse syndrome, occur in 1:1,750-1:13,000 injections.

"Serious" reactions, if defined as permanent brain damage, are even rarer. Consider the following:

Dr. Gordon Stewart, in Scotland: 1:168,000
Dr. Justus Strom, in Sweden: 1:172,092
United Kingdom Dept. Health and Social Security: 1:310,000
Glasgow 1961-1975: 0 in 180,000
London 1977: 0 in 80,000

"Serious" reactions if defined as death are yet rarer, but precise figures are not even estimated owing to the rarity.

- It was stated that studies on complications published from 1933 "have been forgotten." By whom? All texts, advisory bodies, manufacturers, etc., have consistently pointed out that pertussis vaccine can rarely produce brain damage and indicate other side effects.

- Studies were cited by Dr. Justus Strom in Sweden that 1:40,000 children developed "destructive brain damage" after DPT. His more extensive study shows only 1:172,092 suffered brain damage, a deliberately misleading statement.

- Dr. Gordon Stewart claimed his study was ignored by authorities in England. In fact, full details of his study are provided in their document. They disagreed with him, which is not the same as ignoring him.

- It was stated that 1 in 13 children in the UCLA study "had persistent or high-pitched crying after the shot." The study actually recorded the following: persistent crying for one hour or more occurred in 3.1 percent of the DPT group and was characterized by the authors as a "less serious" reaction, as was the high-pitched, unusual cry in 1:1,000.

- The edited interviews throughout the show displayed an emphasis on "proving" the program's negative points rather than obtaining full or informational answers. Examples include unbalanced emphasis on complications, simple partial answers to questions in complex areas and answers taken out of context. Brain-damaged children attributed to pertussis vaccine were shown throughout, but there were no interviews with parents of children who were damaged or died from pertussis itself. This is a blatant example of imbalance; the viewer is only exposed to children form whom he or she must feel compassion without recognizing equal grief in children and parents damaged by the disease.

- It was implied that sudden infant death is caused by pertussis vaccine by citing only part of the manufactuer's package insert, highlighting it in an accompanying graphic. The program ignored the rest of the package insert statement which qualifies the validity of the association. SIDS occurs in infants under six months of age whether or not they get DPT; several studies have demonstrated this.

- The allegation that the Bureau of Biologics does not wish to know adverse reactions is untrue. From my personal experience I can assure you that they are vitally concerned with adverse reactions and labor long and hard to ensure the inclusion in package inserts of adverse reactions.

- It was stated that many doctors are not aware of the risks and reactions from the shots. No evidence for this generalization was given except to follow with a few interviews with parents implying that "doctors" and "interns" are unaware of DPT reactions. To generalize to "many" doctors is fraudulent at worst and deceptive at best. I personally know more than 30 pediatricians in our city and all are aware of the side reactions to pertussis vaccine, as are most of the groups of physicians to whom I've lectured throughout the U.S. in the last 20 years.

There are other examples of bias, inaccuracy and imbalance, but to cite them would be repetitive, as they involve the same or similar areas. My purpose in citing those listed above is to emphasize the impact this program had on its viewers.

The failure to balance the benefits of pertussis vaccine against both the risks of the disease and of the vaccine itself is the major failing. In overstating the case against the vaccine by 1) amount of time devoted to the negatives, 2) editing, 3) editorial comment, and 4) inaccurate presentation of some statistics, the effect has been to undermine public confidence. In the aftermath of the program, many thousands of concerned parents contacted their physicians across the country to reject pertussis vaccine, to question its use, or to report suspected "side-effects" totally disconnected with the vaccine. Wire service reports and local TV station pick-ups and reporting of the Washington show and/or the Today segment amplified this response. Some parents began to question all immunizations and the integrity of their physicians and official governmental and non-governmental bodies.

The major point in all of this is that pertussis is a terrible disease, even if uncomplicated. Children with this illness cough unmercifully, choking in the process and gasping for air. They often vomit and become acutely undernourished and dehydrated. They may destroy parts of their lungs and brain from hemorrhage, lack of oxygen, or both. Further, pertussis is often complicated by disability and death, which have largely been eliminated in the United States by widespread use of a highly effective vaccine. The vaccine is not perfect, does have a number of transient, non-permanent side-effects, but only rarely produces serious adverse effects, and even more rarely does it cause permanent damage or death. The various governmental agencies and advisory professional groups, such as the American Academy of Pediatrics and the Centers for Disease Control, have been knowledgeable about all of the benefits and risks from both the disease and the vaccine and have responsibly transmitted this information to physicians in diverse and effective ways. There has been no conspiracy to conceal facts, nor has there been any attempt to minimize or hide adverse reactions, on anyone's part.

Efforts continue in governmental, manufacturers' and investigators' laboratories to better understand the bacterium that causes pertussis, the body's response to it, and ways to make an equally or even more effective vaccine which has few or no side effects. This is not an easy task and is not readily solvable because the components of the organism which produce host

immune responses also have some toxic properties. Attempts to separate these effects have proven to be difficult and, as of the moment, there is no proved new vaccine.

Pediatricians and other physicians and health workers caring for children have as their primary concern the well-being and welfare of their patients. In using pertussis vaccine they are exercising the best available scientific judgment, which clearly establishes that the vaccine prevents a major debilitating disease but is balanced by some risk. Everything we do for patients must be judged in the same light -- a balance between the risks of what we do against the risk if we do nothing. All medication with whatever product carries some risk. As an individual physician, if I advise a patient to take antihistamine, penicillin, or pertussis vaccine, I am stating that the risk from following that advice is far less than the risk of the disease for which the treatment is advised. For pertussis I am absolutely convinced that the risks from disease are far more numerous and devastating than the risk from the vaccine. I consented that it be given to all four of my children, I advise my patients to receive it, I teach my students and residents about it and recommend its use to them, and as a member of the Committee on Infectious Diseases of the American Academy of Pediatrics continue to advise all physicians to use pertussis vaccine.

The NBC show tended to undermine this balanced judgment and relied upon an imbalanced view, bias and inaccuracies to carry out its destructive message. In my view, this program is not an example of responsible journalism.

Conclusion

Immunization has been an effective medical and public health tool and has reduced or eliminated infectious diseases which once were the scourge of childhood. This effect has resulted from a cooperative effort between government, industry and the private sector. Our efforts today are threatened by decreased governmental expenditures for vaccine, by an unwieldy legal system and by unfair medical sensationalizing of only one part of the total vaccine benefit/risk equation. We should, and must, counter each of these threats to continue to ensure healthy childhood.

Senator HAWKINS. Thank you so much, Dr. Fulginiti.

Dr. Fannin, we want to thank you for traveling from California, and we are deeply interested in your testimony.

Dr. Parrott has to make connections for transportation, and we will excuse him.

Dr. Fannin?

Dr. FANNIN. I am sorry, Senator Hawkins, that you do not have my written testimony. I will have to send a copy of that because I lost my briefcase.

But I listened to the testimony this morning, and many of the things I say in my written testimony have been said much better by other people. And I have to tell you that I subscribe totally to what Dr. Fulginiti is saying and has said; that is my opinion, too.

I am a Board-certified pediatrician, but most recently, I am Chief of Communicable Disease Control for Los Angeles County. This is a county of 7.4 million people. We have approximately 2 million children who come under our purview because they are a major concern in communicable disease control. I also direct the Immunization Assistance Program, which is the name of the Federal-State-local cooperative program for immunization assistance.

Now, I think I will direct most of my comments actually to this program, rather than to the disease or to the vaccine. Since 1965, the Federal Government took a great interest in immunizations, an active interest, investing money in immunization. In the beginning, they started out with a very large quantity of money and then, over time, we have seen waxing and waning interest. Over a 4-year period, you may go to 50 percent of the first year's funding, and then something will happen and all of a sudden, more money will be poured into the program. As I look at Los Angeles County's amount of money obtained through the Federal program, I have noticed this waxing and waning, too. For instance, in 1977 for personnel, we were able to get $400,000. In 1982 for the same program, we are only able to get $259,000 to $260,000. So, in 4 or 5 years, the moneys coming into the county for the program have decreased more than 40 percent. It makes management very difficult.

I know a lot of people have said to me, "But we have really done all that work, and we are almost finished. It is just cleanup time." I think that something everyone needs to understand is that in Los Angeles County, 130,000 new children are born every year. Those children are going to need a certain number of vaccines before they are considered adequately immunized. Half of those children, approximately, 45, 50 percent, will be seen by private doctors in their office, mainly pediatricians, and be immunized there. Fifty percent will require immunization by public programs.

When 50 percent of your population is unimmunized, anything you do is effective, because you have a large number of people unimmunized, and you can hold a clinic, and 3,000 people will come. It is cheap to give the vaccine. When you get down to the last 20 percent or last 10 percent, then it is more expensive per dose of vaccine to run a program, because one, you have to seek out the persons who in fact need the vaccine, so that you do not immunize the same people over and over and over; two, you have to do surveys to give yourself the information you need to run a rational and cost-effective program. All of these things require investment from whomever invests in a government program—it turns out to be the Federal, State, and local governments.

At the present time, Los Angeles County has, we estimate, 2 million children, that is from day of birth to 18 years of age, which is basically our target population for immunization.

You have heard today the statement about 95 to 96 percent of children entering school are immunized against immunizable diseases. Only one word would really make that statement more accurate; that is "public" schools. And I say that, because if you listen closely, that only refers to kindergarten, and it really cannot be applied to the total population of children.

Now, we have done a lot of work in K through 12, kindergarten through 12th grade, to get high immunization levels. In California, we strengthened our law in 1977 and implemented the school immunization law much more vigorously. We have done an excellent job of getting many, many children K through 12 immunized. But we have no good way to measure our birth to 4-year-old, or through 4-year-old age group, immunization levels. We do not have the faintest notion in Los Angeles County what their true immunization level is. That group makes up maybe 200,000 or 150,000 to

200,000 of that 2 million child population. So what we do know, because we do good disease surveillance, or as good as is humanly possible, is that we have changed the epidemiology of a lot of our diseases. And if I can use a case in point, this year, we have had 26 reported measles cases, and that is rubeola, or old-fashioned measles. We have investigated each of these cases thoroughly. Only one of those 26 cases was in a child of 11 years of age; another was in a 16-year-old who was an immigrant after 1977 and was missed by the immunization updating of the high school aged student. But three-quarters of those cases were children 4 and under, with measles. And a fairly large number—I think about five—were adults, people 20 and older, who had measles.

Now, I call it measles because we verified literally by doing serum testing that, in fact, the disease they were having was not just any rash illness, but was rubeola.

Another factor we looked at was, was the disease imported into our community? Or did it just spontaneously arise in our community? Unfortunately, we could not find a source in approximately 50 percent or 13 of those cases; but in 9 of those cases, there was a direct out-of-the-country connection. One was a traveler from Germany, and the other 8 had connections to Mexico. They literally either arrived with their disease from Mexico, or they visited in Mexico at the point in time when they must have been exposed to the disease. So, that tells us that in our county one problem with measles elimination among the various other problems is importation from all over the world and from other states. We have to deal with that, too.

One thing that is very comforting, and probably is reflected by most of the cases occurring in the zero to 4 age group, we have had no major outbreaks. The largest group of those 26 cases who were related to each other was 3, and they were 2 siblings and a cousin of those siblings. We have had three cases in schools with no spread. So that reassures us a great deal that our basic immunization level for this disease is very high.

But, we have 26 known cases of measles in our community, and if we surround those cases with susceptibles, we will have 26 outbreaks from those cases. It is a highly contagious disease, and in a group of susceptibles, the attack rate is very high, because it is spread by the respiratory route. It is a virus. There is no way to prevent it by taking an antibiotic after exposure.

So I think we are where we are because of a vigorous involvement by Federal, State, and local government, and I think we have to fight to keep the advances we have made, and we have to be realistic instead of picking this little fact from this place and that little fact from that place. We have to try to get a balanced view. I think that you are getting a pretty balanced view of many of the issues, and I hope that your Committee minutes are going to be published somewhere.

Anyway, so back to the issue of funding, many things are eroding funding, and whether one realizes it or not, the cost of vaccine is a major one. My budget says that I still get $300,000 worth of vaccine. You notice it says "dollars". It did not say 300,000 doses of vaccine. When the cost of a single dose of vaccine goes up 29 per-

cent, the amount of vaccine that I get for that $300,000 goes down 29 percent.

Senator HAWKINS. Why should it go up 29 percent, in your opinion?

Dr. FANNIN. I do not understand all the ins and outs of that. But I have been a bit fearful, as we have looked at vaccine manufacturers leaving the field that we were getting to a point of no competition.

Senator HAWKINS. Single source.

Dr. FANNIN. I am not very comfortable with that.

Senator HAWKINS. I have great concern about that, as I have expressed before.

Are you able to reach and immunize the illegal immigrant?

Dr. FANNIN. Well, the illegal immigrant or the legal immigrant ultimately send their children to school; the vast majority do. Our school immunization law requires that with first school entry in California, you must provide proof that you are immunized against the seven childhood diseases that are vaccine preventable. So, yes, we do. And we get a great deal of cooperation, especially from our Mexican, Central and South American immigrants. When it is presented to them, they are very happy to get the immunization.

Senator HAWKINS. Do you agree that the decrease in the number of susceptible children, improved program efficiency and widespread public involvement in the immunization program will more than offset any decline in the purchasing power of Federal funds?

Dr. FANNIN. Federal funds have never bought immunization for any community. When I tell you that we give between 750,000 and 850,000 doses of vaccine to children, and when I tell you that we get less than $500,000 of assistance in a good year from the Federal Government, those vaccinations do not cost 25 cents apiece. So the county of Los Angeles and its citizens pay all but the 25 cents per vaccine cost. So we are only getting assistance. But local government has problems with the waxing and waning assistance, and with the problems that we have anticipating in any one year what next year's budget is going to be. It has been very difficult to keep up with this mechanism of changing budget every year.

Now, I looked at the 1980–81 budget, just to track and demonstrate to you what happens to money from the Federal Government to the local government. That year, the Federal Government—and it was my understanding that the Congress voted for $36 million—somebody said $45 million—finally appropriated $24.5 million. And we are talking about a total, 50-State allotment—$24.5 million. That translated in the State of California, which makes up 10 percent of the total U.S. population, to $1.8 million, from the Federal Government to the State government. Our State government added to that another $1.5 million. Anyway, the total was nearly $3.8 million. Los Angeles County, which is 33 or 34 percent of the total State government, got 20 percent of the available money that came from the State of California for immunization.

Now, for the target population of childhood, we literally make up more like 40 percent of the State population. So it really gets rather thin at a local level. I do not want to fight with the Federal Government and the State government over funds. I think that there are not enough funds being given to any State to do a realis-

tic job—you know, we set our goals, 90 percent by 1979, and eliminate measles by 1981, all of this—totally unrealistic goals in the face of the vagaries of funding. If you want me to eliminate measles in Los Angeles, you must send money. I am not going to do it on the back of the other parts of my program. Well, it is unreal to think you are going to buy all these wonderful things for the amount of money we are investing in it. The inflation factor added to the dollar cost cause yearly need for budget increases. My program lost 25 percent funding between 1979–80 and 1980–81. Then, between 1981 and 1982, the State kept the level the same—exact same dollar amount—which in effect with inflation was a decrease. But it all looked very good. We got the same dollars as we did last year; 2 months into the first 6 months, I was told we would have to renegotiate a second 6-month contract because they were not going to get the money from the Federal Government they expected. So my program took a 22-percent decrease from the first 6 months to the second 6 months of funding, added was the extra money it cost the program to do those contract negotiations.

Very frankly, we are getting to the point where we almost cannot afford the money you give us. But it is not a charitable dollar. We are citizens. We do the work of getting vaccine in arms. There would be no reason for anybody to be funded at any other level of government if we do not get vaccines into arms at the local level. We make the program cost effective. We decrease the disease rate by the number of doses of immunizations we give. We need CDC, we need the State government and their input. We need Dr. Fulginiti and his committee, because they give us the information we need to reassure ourselves that we are doing the right thing and that the decrease in disease levels is reflecting a good in our society, a good of science.

I would not want to see the CDC program under Dr. Hinman be decreased. They do a valuable service for us. We cannot get along without them. But I must have money also to get immunizations into arms. If we do not, it will take 3 to 5 years, maybe, for the curve of disease to start in the other direction. We have not wiped out any disease except smallpox. The others are in check because we have high immunization levels, and low susceptible populations.

I heard somebody mention eliminating measles. I have to laugh, because as a pediatrician, as an infectious disease person, I know measles is not smallpox. We may be able to control it by giving lots of vaccine, but no one else in the world is controlling their measles, so we are not going to eliminate measles in the United States. It would be nice, but we are not going to do it. The proof of immunization of measles is not written in a scar on your arm. Your immunity from the disease is not written in scars on your face. So I think we are a long way from doing the same thing with measles that we did with smallpox.

Senator HAWKINS. Would you briefly describe the California legislation which requires the State department of health to reimburse the medical expenses incurred per child as a result of a severe reaction to a State-required immunization?

Dr. FANNIN. Yes. In California, when we tightened up our school immunization law in 1977, we also felt a responsibility to our citizens that they be protected when the State required something to

be done for the good of the State or the community. We felt if there were damages that might accrue to a child from that requirement, that the States should, then, compensate.

We do have a law that will compensate up to $25,000 for any immunization-associated injury for the seven childhood diseases required by our law to enter school.

[The prepared statement of Dr. Fannin follows:]

CHILDHOOD IMMUNIZATIONS May 7, 1982

TESTIMONY OF SHIRLEY L. FANNIN, MD, CHIEF
COMMUNICABLE DISEASE
LOS ANGELES COUNTY DEPARTMENT OF HEALTH SERVICES

AT

SENATOR HAWKINS' INVESTIGATION AND GENERAL OVERSIGHT SUBCOMMITTEE
OF THE SENATE LABOR & HUMAN RESOURCES COMMITTEE

The Immunization Assistance Program, funded by the federal government since 1965, is based on the premise that immunizations are a legitimate and cost effective way to decrease childhood morbidity and mortality. At the outset, there were large numbers of children who were not protected against the vaccine preventable diseases. In fact, among the less fortunate groups in our society, probably less than 50% of children were protected.

The first years of the program were spent in developing a functioning team and seeking standard measurements of program effectiveness. They were also marked by the introduction of effective new vaccines--live measles vaccine in 1967, mumps vaccine in 1968, and rubella vaccine in 1969. The introduction of these vaccines led to a major program effort to get as many children as possible protected with each new vaccine. The funding and programming tended to concentrate on one vaccine at a time but did not fully address the issue of total population immunization as a goal.

In the mid-1970s, many states were moving toward school immunization laws. It has been recognized for many years that grade schools were the major source of community spread of the childhood diseases. Unless that population were almost fully immunized, disease levels would almost surely remain at a high endemic level with periodic epidemics sweeping through the community.

The communities concentrated on improving surveillance so they could develop expected levels of disease against which program effectiveness could be measured.

In California, school immunization law was not effectively implemented until the mid-1970s. In 1977, Los Angeles County, along with other areas in the country, had a worse measles epidemic than any year since 1972. This provided the opportunity to bring the need for better and more effective implementation of school immunization laws into focus. The public supported the concept that children should not die or be permanently damaged by a disease that could be prevented by immunization.

Since 1977, Los Angeles County has accomplished an overall 90% or better immunization in the public schools, K-12 population. This has been sufficient to decrease the incidence of vaccine preventable childhood disease to all-time lows. We have not had one case of reported tetanus in a child since 1978, not one case of reported paralytic polio in a child since 1975. In 1981, we had 126 cases of measles 158 cases of rubella and 122 cases of mumps reported from a population of approximately 2 million children. The epidemiology of disease has changed significantly so that the majority of reported cases are occurring in the 0-4 age group and in young adults.

The job of immunization is not finished. The segment of the population most at risk for severe complications and death from childhood diseases are the 0-4 age group. These children have not been immunized to a 90% level, in fact, I would be surprised if they are even 60% immunized overall. The only ones in this age group we have been able to confirm as immunized are those who are in licensed day-care centers or in government-sponsored head start programs. We have eliminated none of these diseases. We are merely keeping them at low levels because of high levels of immunity. Maintaining these advances will require ongoing support from the federal, state, and local government.

Funding for immunizations has been decreasing to the local level for the past several years. For instance, in 1980-81 fiscal year, we had a 25% cut in funding for personnel. In 1981-82 fiscal year, we received funding at the same level as the year before for the first six months and had a 21% cut in personnel funds for the second six months. When the effect of inflation is added, the full impact of these cuts is obvious.

Another very significant factor that modifies the federal dollars in the Immunization Program is the 29% increase in vaccine cost imposed by vaccine manufacturers

this year. This, in fact, significantly decreases available money. We have been warned that another large increase in vaccine price is due this fall. Being at the mercy of a budget that does not expand and rising costs that are out of our control, we find good management difficult to impossible.

Los Angeles County Department of Health Services has shifted resources to keep the Immunization Programs viable. At present, the County government is having difficulty finding resources to cover essential services. It is doubtful that we can expect many further shifts of resources. There will inevitably be significant slips in a productive and very cost-effective program.

If you ask me how to solve the problem, I can only suggest more funding for immunization from the state and federal government.

Centers for Disease Control is essential to successful local immunization efforts. We look to them for technical expertise and research that keeps us abreast of latest developments in the field. I would not like to see their programs cut.

The state health department also provides technical assistance to local programs, and at times of urgent need, even more direct assistance. I would not like to see their programs cut either.

Suggestion has been made that Immunization Programs seek funding from the Maternal and Child Health block grant to the state. I have been told that California will be receiving 2 million dollars less in this block grant than previously allocated. If I presume that programs heretofore funded under this grant are good programs, I must also presume that they will receive first priority for funding. As creative as my imagination can be, I cannot see buying so much more for so much less. This, then, does not appear to be a viable option.

What will happen if Congress continues to withdraw funding from the Immunization Program? The programs will ultimately deteriorate resulting in decreasing levels

of immunity. Increasing morbidity and mortality will negatively affect the economy with increasing medical costs, lost wages for working parents who stay home with their sick children and rising costs of rehabilitation for those left damaged by diseases that are preventable. This outcome will not take a generation to happen but will happen within five years after significant program deterioration occurs.

Surely, in a budget that can pay 23 million dollars for one small plane, a few more million dollars for immunizations to help protect our children is not too much to ask.

Senator HAWKINS. Thank you very much. Your testimony will help greatly in aiding Congress and the Department of HHS, which comes under our jurisdiction. Keep up the good work, and I hope you find your briefcase.

Dr. Munzer, you are here on a topic of vital concern to me. I know there is no vaccine against tuberculosis, but you are prepared, I am sure, to give us a brief statement about the difference between tuberculosis and other infectious diseases from the public health standpoint.

Dr. MUNZER. Thank you, Madam Chairman, and members of the subcommittee. I am a physician specializing in diseases of the lung and chairman of the Tuberculosis Committee of the District of Columbia Lung Association, and a member of the board of directors of the American Lung Association and the American Thoracic Society, and I am delighted indeed to have this opportunity to address the status of tuberculosis control in the United States.

Just 100 years after the discovery of tubercle bacillus and 30 years after the development of effective therapy, there still are 28,000 new cases of tuberculosis annually in the United States.

In 1980, for the first time since 1963, the number of new cases of tuberculosis exceeded those in the preceding years. Tuberculosis is five times more prevalent among nonwhites than whites. It is concentrated in low-income, urban areas, and in Washington, D.C., the Nation's Capital, and Newark, N.J., the incidence is four times the national average. Baltimore, Detroit, Birmingham, New Orleans, Tampa, have a case rate three times the national. The influx of refugees, furthermore, has been responsible for an increase from 333 cases in 1979 to 417 in 1980 in Miami-Dade County, Fla., and from 358 to 493 in San Francisco.

In 1981, Massachusetts, with 504 new cases, experienced its first upturn in tuberculosis in over 20 years. The 11.5-percent increase is the largest since 1915. Tuberculosis among adults for the most part represents reactivation of infections acquired many years earlier. Tuberculosis in children, however, is a result of recent transmission of the disease and indicates a failure to control spread of the disease by such public health measures as contact investigation, case followup, and preventive therapy. In 1980, there were in fact 893 cases of tuberculosis among children under the age of 5, and children still die of this totally preventable disease.

What has been the response of the Federal Government to the resurgence of tuberculosis? In 1980, State health departments reported the expenditure of approximately $9 million in funds allocated to tuberculosis under formula grants authorized under section 314(d) of the Public Health Service Act. That authority was withdrawn on October 1, 1981.

The Omnibus Budget Reconciliation Act of 1981 authorized for preventive health service programs in tuberculosis, the appropriation of $9 million for the fiscal year ending September 30, 1982, $10 million for the fiscal year ending September 30, 1983, and $11 million for the fiscal year ending September 30, 1984. It is sad that no funds thus far have been appropriated. The full amounts should be appropriated so that progress can be made toward reducing the case rate of tuberculosis in the United States to 8 per 100,000, the goal set forth by the Surgeon General.

Madam Chairman, the American Lung Association, and the old, the poor, and the infirm, who are particularly susceptible to tuberculosis, appreciate your personal and this committee's efforts to rescue tuberculosis not from the tubercle bacillus, but from political indifference.

Senator HAWKINS. We are trying our best to get that money back, Doctor. If we were able to do that, how would the money reach the recipient? I hear from my colleagues that there is a lot of money spent in the program and not much on the patient.

Dr. MUNZER. The great advantage of having categorical grants rather than bloc grants is that funds can be targeted to areas where there is the greatest need, and the act does give authority to the Secretary of HHS in consultation, I would assume, with the CDC, to target those funds. And with tuberculosis, that is precisely the problem. We are dealing with specific areas that have a very high incidence.

Senator HAWKINS. How accurate are the statistics with respect to the incidence of tuberculosis and the effectiveness of control measures?

Dr. MUNZER. Recently, in the District of Columbia, there was a report of a marked decrease in the incidence of tuberculosis, a 30-percent drop. That kind of drop, by virtue of the biology of tuberculosis, is impossible, simply because most cases of tuberculosis originate from infections that have been acquired many years earlier, and unless all those susceptible individuals have been eliminated, the case rate simply cannot drop.

As a result of that drop, I contacted the Centers for Disease Control, to ask whether they are in a position to either confirm or verify the data that is obtained from local health departments, and the answer basically is no. So the only thing that happens when data are at variance, when they show a 10-percent change, is that a letter will be addressed by CDC to the local health department. At the present time, there is no automatic audit. There is no check to make sure that the definition of cases of tuberculosis has not been altered, for example.

So, to answer your question, the data are unreliable at present.

Senator HAWKINS. What are the priorities of tuberculosis control?

Dr. MUNZER. The first priority is the treatment of patients with active disease and eliminating them as a source of infection to others. The second is careful followup of these cases. Tuberculosis must be treated over a long period of time. It takes 9 to 18 months to treat a case of tuberculosis, and it is very difficult to motivate a patient to continue taking medications for that length of time, and close followup by a health department, therefore, is important. The third priority is preventive therapy of those individuals who have come in contact with a case of tuberculosis and who have been infected, so that they will not develop disease and become vectors of further disease many years later.

Senator HAWKINS. We really appreciate your contribution, Dr. Munzer, and hope that we will be able to work closely with you in restoring the funds that are so vitally needed in tuberculosis control by my State, California, and Washington, D.C., and of course

will be most grateful if we are successful. We appreciate the scientific evidence that you have brought to this hearing today.

We really want to thank all of those who have participated today. There are many questions, I am sure, that are left unanswered. The reason that the Subcommittee on Investigations exists is so that those questions that need to be answered will be pursued at further hearings.

We all know what childhood immunization has meant in terms of prevention of human pain and suffering, and I would urge all parents not to abandon—I must repeat that—I would urge parents not to abandon this most vital program. The concerns expressed here today, however, are valid and need to be addressed.

I decided I must be middle-aged, because I had all the childhood diseases, experienced them in my home, and listened to the whoops that the doctors described today. I have a daughter who had a reaction to DPT, and it is a lifelong reaction. She is the new mother of our new grandson and she did have some complications because of the breathing problems that she has in her lungs. I have a son who had polio after he was immunized with the polio vaccine. Very luckily, and with a year or two of tremendous therapy, he was restored from a paralyzed state to being completely healed with a slight limp, and is a six foot four tremendous specimen today. We were very fortunate and the Lord was very good to us, along with good doctors and great counsel.

My husband, the youngest of six children, came from a very loving family. His father died when he was 2. The children shared bedrooms and lived in very close, crowded conditions, in a low-income neighborhood. Yet, none of those children ever had any of the childhood diseases. He has never had the mumps, and he is panicked today because one of our grandchildren might get chicken pox, and he does not know his chances of contracting them. We think he has permanent immunization, but we have learned that sometimes that declines as you age.

So, as I sit here listening to this, I can put myself into everyone's shoes who has testified. I must say that as a responsible citizen and as a mother of children and a grandmother, it is my hope that this hearing will expedite a rapid development in testing of the safest possible vaccine, and the accumulation of the most reliable statistics on adverse reactions and immunization rates. In a public health clinic, perhaps the only feasible means is a printed sheet of paper, disclosing the risks and benefits of the immunization. I think it should be as precise and as comprehensive as possible and the reading of it and the signing of it should be a prerequisite of getting the immunization.

I think that we must work more closely with the private physicians to insure that they distribute the same documents and that it is read by that parent or whoever brings in the child. I am afraid that we are letting some children slip through our fingers in the private immunization segment of our population.

Trained personnel should be available. I have been in these clinics. They are so crowded, and the kids are all crying, and by the time it is your turn to get the shot, you just want to get in and get out of there, and take the screaming infant with you. There should be trained people speaking with parents, and giving and explaining

these documents. Trained personnel should be available because in some instances, the doctors and nurses are just too busy expediting the long lines. This is especially so just before school starts, when you have to have that piece of paper documenting the immunizations.

It is equally important that the private physician sit down and speak with the parents. I just cannot overemphasize that. I happen to have had a lot of discussions with physicians since this hearing was set—and I must say, this hearing was set long before the television program; it was not in response to the television program that has been mentioned so many times today. I was one of two Republicans who voted to restore the funding for the immunization program when it was recommended that it be cut last year. We wanted to have hearings to provide evidence to my colleagues that it should be restored. It was just coincidental there was some publicity on adverse reactions. But I believe that a lot of the things that have been said here today will result in a better world. I think we all now know that we need better vaccines, and I think that we have begun to see a more realistic picture of the risks and the benefits.

There is no doubt that we need to gather and disseminate the most reliable information on adverse reactions as widely as possible, perhaps through public health announcements. I think we must tell parents both sides of the story, and we must also remind them of the great epidemics that we used to have. I can remember the times when I was growing up when all the swimming pools were closed each summer because polio was so widespread. There would be bans on movies and you could not go to the movies during the summertime because of an outbreak of polio. We want our younger parents to realize that there have been epidemics with horrendous results, leaving people crippled for the rest of their lives. We have a Senator among us today, Senator John East, who is in a wheelchair and serves very ably and very well, but is crippled because of polio.

I would like to thank all of you who came here today to tell us your experiences and to give us necessary advice. We are grateful for the expertise and the personal experiences that were shared with us. Some of those experiences are very private, and we appreciate what you have related.

We leave here today, I think, with the knowledge that a constructive dialog has begun, and that we will continue to protect the health and the lives of our children.

At this point I order printed all statements of those who could not attend and other pertinent material submitted for the record.

[The material referred to follow:]

# TESTIMONY OF

# ISABELLA B. GELLETICH

# BEFORE THE

# COMMITTEE ON LABOR AND HUMAN SERVICES

MAY 7, 1982

I am the mother of a mentally retarded, severely psychotic, 18 year old innoculation victim. There has never been a history of mental retardation or genetic schizophrenia in mine or my husband's family.

Let me start by telling you exactly what happened to my boy. Michael was born on August 25, 1964 and was diagnosed as a healthy, normal baby by at least three competent physicians; they were my obstetrician, the staff pediatric resident and my own hired pediatrician. My baby was very carefully checked for flaws because there had been a German Measles epidemic during my pregnancy.

Michael was a small baby only weighing 5 pounds 7 ounces with a delicate bone structure indicative of my paternal grandfather's family. He didn't like to eat much and feeding him was a chore but other than that he was a sweet, quiet and affable baby that reflected the poise and reserve of his father's family.

On June 22, 1964, two months after his birth, during his first well baby visit to the pediatrician, my son was given his first injection. It was done despite my mild objections and protestations that the baby's diminutive

size of approximately seven pounds was adequate reason to put off the start of immunization. I was told that the innoculation had to be started to protect my child. I have relived that scene in my mind a million times during these past 18 years because those were the last quiet and secure moments I would ever know with my child. The baby became fussy but eventually fell asleep that night. From that point on I had difficulty waking him for feedings.

Around noon on June 23, 1964 I discovered that my son had a fever of 105.3 degrees. He was hospitalized and that afternoon experienced several hours of unremitting screaming so severe that I couldn't bear to hold him and my husband had to walk the floor of the hospital room with the child. I pleaded with the nurses to do something. One nurse told me, off the record, that my son had exhibited the symptoms of sudden infant death syndrome and that it was being theorized that I had saved his life when I discovered the high fever. I was never told that the screaming was indicative of brain damage. I had to gain that information from a T.V. program 18 years later.

The next day, after my son's fever had abated my doctor released him from the hospital telling me that the baby was fine. When I directly questioned the doctor

as to whether or not the shot he had given my son could have caused the trouble, he said that he would never give my child anything that would hurt him.

From that point on my son was hyperkinetic, never really knowing one moment of physical quiet and contentment. Within the next week I noticed that both of the baby's eyes turned in, producing the classic cross-eyed syndrome and within 30 days he was diagnosed as having severe strobismis. These symptoms I now know can be indicative of brain damage. In the hectic months and years that followed I was carefully led to believe by deliberate categorical lies alluding back to the measles epidemic that my son had been born defective.

What followed these incidents has been 18 years of helter-skelter searching throughout the entire east coast medical community to get help for my boy. It has been a futile attempt to make him whole again. Years of unrelenting work. Years of agonizing anguish and pain for him and for all of us that love him. Yes, we taught him to speak and to read and write, he can even ride a horse and swim and dive, but by last year we could no longer physically control his violent and unpredictable behavior and we had

to petition the Courts of Fairfax County, Virginia to commit him to a mental institution while we waited an inordinate amount of time for the Fairfax County School system to place him in a residential facility. We used up over $50,000 worth of health insurance benefits and personal funds in that 18 week period.

Now, after the fact, the medical community will try to tell you and me that my son is a statistic. They will say that Michael is one in 70,000 or one in 70 million. They will tell you that this is an acceptable risk to protect the masses from disease. If that is so then my boy and all the other young men and women like him should be as honored as the heroes that landed on Anzio Beach. They have given up all semblance of a normal life so that others could be healthy. Instead, they have been robbed not only of their brains but even of that last vestige of dignity, the right to know the truth.

My son was not listed as a vaccine statistic at the time of his damage and I now have logical reason to believe that my doctor deceived me. How can any of us put our faith in the medical profession's statistics when they are obviously based on lies and cover ups?

I am not alone in this. In recent years I have noticed that I can walk into almost any public function and find one or more parents of brain damaged individuals. Since viewing Lea Thompson's show I have been mentally ticking off the names of people close to me that have experienced one degree or another of brain damage symptoms in their children. Many of the women I grew up with are raising brain damaged children. For years I have wondered why God had placed his hand on so many of my dearest and closest friends and their families. The frightening answer could be that God didn't do it. What I am scared to death of is that hundreds and thousands of children have been brain damaged by man's greed and inadvertant lack of attention to detail.

The medical profession's credibility has been seriously and effectively challenged by the Lea Thompson Report on Vaccine Roulette. Parents all over the country are going to have a difficult time perceiving the truth and the whole structure of our legally prescribed innoculation program is going to be eroded by fear and lack of confidence. The private sector can not be expected to clarify this complex issue; it therefore falls upon our Government to do something definitive about it.

I ask that my Government do expeditiously two things. First, conduct an immediate and vigorous comprehensive study to gain the facts about the level of damage that truly exists from innoculations. Second, regardless of the statistics that emerge, institute a federal innoculation compensation program for the injured. You can not realistically expect the medical community to honestly report injuries while the threat of law suits hangs over their heads; and, you should not expect children to give up their most precious commodity, their brain, for the good of the majority while you then turn your back on them in the years of tragedy and struggle that will surely follow brain trauma. I am here as living testimony to the fact that the present education laws that protect brain injured children are totally inadequate and do not address their life long needs. At age 22 many of these people are dumped on an uncaring and unsympathetic society. Their friends and parents are then forced to struggle with local authorities in an attempt to obtain adequate living conditions for these diminished adults.

Someone once told me that in the face of irreversible tragedy, first you cry. Well, they were absolutely right.

I thought that in the last 18 years I had shed every tear I had left in me but much to my shock after I viewed the Lea Thompson Report I cried, not a little but a lot, days and nights of uncontrollable tears. I wanted to scream and I wanted to stop the pain of truth. Deep down inside I was hysterically aware that under the innoculation controversy could be hidden an American Holocaust with thousands of our precious children damaged. I have spent 18 years on the inside of programs for the brain injured. Now I wonder, are my son and I the survivors of a modern day Auschwitz, both of us left crippled and maimed by apathy and deceit. I only pray that someone in my Government will prove me wrong.

Thank you.

Isabella B. Gelletich
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Annandale, Va., 22003

CASE WESTERN RESERVE UNIVERSITY • CLEVELAND, OHIO 44106

June 3, 1982

The Honorable Paula Hawkins
1327 Dirksen Building
Washington, D.C. 20510

Dear Senator Hawkins:

I am writing in response to a conversation that I had with a member of your staff regarding the current concern about pertussis vaccine, which was stimulated by a most unfortunate and inaccurate program put together by NBC in Washington. I should like to comment about vaccine programs in general in the United States and upon pertussis vaccine in particular. Though I speak as an individual, I have been a member of the Committee on Infectious Diseases of the American Academy of Pediatrics for 16 years, and served as its chairperson for three of those years. It is this committee that makes immunization recommendations followed by pediatricians in the United States and in many other countries. I have been a liaison representative of the American Academy of Pediatrics to the Surgeon General's Advisory Committee on Immunization Practices for several years as well. Finally, I served as a member of the Panel on Bacterial Vaccines of the Bureau of Biologics and continue to serve as a consultant on vaccines to the Bureau. Thus I believe I am well qualified to discuss the benefits and risks associated with vaccines.

The success of vaccine programs in the United States is too well known to belabor. If, in the absence of poliomyelitis vaccines, the experiences of the years 1950-52 had continued to the present, we would expect about 75,000 cases of poliomyelitis annually, with nearly 5,000 deaths and approximately 10,000 individuals ending up with respiratory impairment that would have required the use of the old iron lung or its equivalent. Now, if we have ten cases of poliomyelitis a year in individuals who escaped immunization, we consider it a bad year. Because of immunization, diphtheria and lockjaw are essentially unheard of. In 1964-65 about 20,000 newborn babies were permanently handicapped by German measles which their mothers had early in pregnancy, and another 20,000 infants (perhaps more fortunate) were stillborn or spontaneously aborted. Because of rubella vaccine, developed and widely used starting about 1970, we have prevented a recurrence of this problem. Without measles vaccine sooner or later every one of the three and a half million kids born in this country annually would develop the disease; about one of every 1,000 of these or 3,500 would develop measles encephalitis as a result among whom about 350 would die and about half of the remainder incur permanent brain damage. Measles vaccine has changed all of this.

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*Chairman, Department of Community Health*

But none of these vaccines is absolutely perfect, though diphtheria and tetanus toxoids come pretty close. Four or five cases of polio a year are caused by oral polio vaccine. From German measles vaccine some individuals get unpleasant, though transient, arthritis lasting some weeks or a few months. Measles vaccine induces a tragic and distressing encephalitis, called Dawson's encephalitis, in about one of every million recipients (the disease caused it about ten times as often). Though it is therefore obvious that the benefits of these vaccines enormously outweigh the risks, every effort continues to be made to reduce these small complication rates.

The success of the widespread use of pertussis vaccine as a public health measure is also well known. Last year there were seven deaths from whooping cough in this country; based on experiences in other countries and extrapolation from what happened here prior to the vaccine suggests that we would have 1,000 or more deaths annually if the vaccine were not available. At least an equal number of children and probably many more would incur permanent brain damage as a consequence of the disease, and it is impossible to estimate the amount of suffering and other problems that would accrue as a result of widespread outbreaks.

But there is no question that the vaccine is not perfect. Our best estimates are that, of the three and a half million children born annually in the United States, between 20 and 35 incur permanent brain damage as a result of the vaccine. Each of us concerned with vaccine recommendations believes that this is 20 to 35 kids too many.

Why does the vaccine produce such damage in a small number of children, and why hasn't something been done about it? The answer to both questions is really rather simple. The pertussis organism (the bacterium that causes the disease) has been a very difficult organism to study and understand in terms of what parts of the organism do what. This is in contrast to many other bacteria, such as the pneumococcus that causes lobar pneumonia. Accordingly, because we haven't known what it is about the bacterium that makes people sick and what part of the bacterium it is that makes people immune to further infection, it has been impossible to prepare a "purer" vaccine. This is not because people haven't tried; an enormous amount of time, money and effort has been devoted to trying to unlock the secrets of this bug.

But within the past decade progress has been made at long last. The organism has been "taken apart", so to speak, and it is much better understood. Indeed, because of technology now available, it is likely that we shall have a "purer" vaccine in the not too distant future. It won't be tomorrow; much more remains to be done, but the techniques that will lead to success are available.

One of the things that distresses me about the NBC presentation is that it came across that somehow the U.S. scientific community was hiding its head in the sand or, alternatively, was keeping the facts about pertussis vaccine hidden from the public. Moreover, the program suggested that nobody in the U.S. had really been concerned about, or interested in, pertussis vaccine. None of these could be

farther from the truth. For example, the Panel on Bacterial Vaccines of the Bureau of Biologics started considering pertussis vaccine in detail eight years ago. All information related to the vaccine and its use in the United States and in other countries, as well as problems about its reactivity, were considered and studied in detail. Indeed, it was the Panel that suggested the study that was ultimately sponsored by the Bureau of Biologics at UCLA. Early in November of 1978 the National Institutes of Health and the Bureau of Biologics sponsored a three day international seminar in Bethesda which was totally devoted to pertussis vaccine and the disease, including the epidemiology of the disease, the effects of the vaccine, the risks of the vaccine and progress toward the development of a newer vaccine. The symposium was attended by authorities from all over the world, including Britain, Russia and Asian countries. The symposium was well attended by the press and within a few months the entire symposium was published in book form. This book has become more or less of a standard reference on pertussis and pertussis vaccines.

Thus, the scientific community, both within and without the federal government, has not been idle in its consideration of pertussis vaccine and means to develop a better preparation. Therefore I am distressed by the possibility that the Congress, which obviously cannot be aware of all of the efforts that have been conducted in an effort to find ways to develop a better vaccine, will be swayed by NBC's rather emotional expose, and divert the efforts of the scientific community from trying to do their job to develop a better vaccine into less productive avenues of explaining what has already been explained. What is most important is to provide the support for basic scientific efforts to improve the vaccine.

You may be interested to note that, at least in the Cleveland area, it appears that there will be very likely no important effect on rates of whooping cough immunization as a consequence of what I believe to have been an extremely irresponsible piece of journalism. Although great consternation was caused many parents, spot checking with seven pediatricians has turned up only one parent who refused pertussis vaccine for a child in the past month and a half among hundreds due to be immunized. I sincerely hope that the whole thing has been sufficiently defused that we shall not repeat the British experience.

Yours,

Edward A. Mortimer

/cr

STATEMENT

by

J. Anthony Morris, Ph.D., Vice-Chairman
The Bell of Atri, Inc.
(A Public Interest Organization Concerned with
Health, Science and Public Policy)

to the

SUBCOMMITTEE ON INVESTIGATIONS AND GENERAL OVERSIGHT

COMMITTEE ON LABOR AND HUMAN RESOURCES

UNITED STATES SENATE

WASHINGTON, D.C.

Hearing held: 7 May 1982
Statement submitted: 30 June 1982

96-132 O—82——10

I appreciate the kind offer made to me by the staff of the Subcommittee on Investigations and General Oversight to add to the record of this Hearing.

Senator Paula Hawkins in her Opening Statement said ". . . The immunization program is now threatened on another front--the fear of adverse health effects resulting from immunization. To combat this fear and to achieve and maintain high immunization rates, full public communication and health education is essential. The general public has a right to be given information about vaccines--even in areas of scientific and medical uncertainty. We must present the issues to the public clearly and accurately."

In light of Senator Hawkins' remark that ". . . We must present the issues to the public clearly and accurately . . .", I would like to comment on the testimony given before this Subcommittee today by Dr. William H. Foege, Centers for Disease Control, Atlanta, Georgia; Dr. Vincent A. Fulginiti, American Academy of Pediatrics, Tucson, Arizona; Dr. Robert Parrott, Children's Hospital, Washington, D.C.; and Dr. Shirley Fannin, Department of Health Services, County of Los Angeles, California.

Dr. William H. Foege. Early in his testimony, Dr. Foege said that "In the fall of 1980, 96 percent of children entering school for the first time had been protected against DTP . . ."

The quoted statement is meaningless and misleading, for later in his testimony Dr. Foege said "Since antibody production alone is not a consistent indicator of immunity to pertussis, vaccine efficacy is primarily determined by protection conferred by vaccine in the face of exposure to disease. Recent studies of the effectiveness of currently available pertussis vaccines carried out in the United States have indicated a vaccine efficacy of 63-94 percent." Dr. Foege in his testimony had already said "The low incidence of pertussis disease and the apparently (underscoring mine) good protection offered by the current vaccines make clinical trials for efficacy very difficult in this country."

At no place in his testimony does Dr. Foege give the informational base for his assertion that "96 percent of children entering school for the first time had been protected against DTP . . ." and without this informational base there is no way to determine the validity of the expression "96%."

Dr. Foege said, further, that "The Food and Drug Administration recently supported a study at the University of California . . . Among those children receiving the 15,752 doses of DTP vaccine administered in this study, 9 had convulsions . . . 9 had episodes of collapse, a frequency for each of these conditions of 1 per 1,750 immunizations. No cases of encephalopathy occurred in this study."

Dr. Foege failed to mention that in this FDA supported University of California study that 2 infants died of apparent sudden infant death syndrome within 96 hours of DTP vaccination and that the authors of the report of the study concluded that ". . . in any 96 hour period approximately 1 in 15,000 infants in the age group would be expected to die of SIDS. Therefore, two such deaths in this series are not unexpected. However, this does not exclude an etiologic relationship between DTP immunization and SIDS" (underscoring mine).

Next, Dr. Foege submitted for the Hearing record a table of the recommended immunization schedule for children showing that the first injection of DTP should be given at 2 months, the second at 4 months and the third at 6 months (and a fourth at 18 months and a fifth at school entry). In his testimony, however, Dr. Foege said that "At present 95% of children entering

school have evidence of having received at least 3 doses of DTP (or DT) vaccine . . . It is important to note that a minimum of two doses (and probably three doses) is needed to induce protection at the 70-90 percent level" (underscoring mine).

If, indeed, it is important to note that a minimum of 2 doses and that it is only probable that 3 doses of DTP vaccine are needed to induce protection at the 70-90 percent level--then, Dr. Foege did not specify in his testimony why the 3-dose schedule is the recommended procedure.

In my judgement, Dr. Foege's testimony fails to meet the requirements called for by Senator Hawkins in her opening statement that "We must present issues to the public clearly and accurately" and that "There must be candid disclosure of the risks as well as the benefits of . . . vaccines."

Dr. Vincent A. Fulginiti. Dr. Fulginiti testified that "Currently there are a number of threats to [an] effective system for control of these diseases [measles, mumps, rubella, diphtheria, tetanus and pertussis]. Among them are: 1) reduction in federal funding . . . 2) legal suits . . . 3) sensationalism of reports of damage secondary to vaccine presented by the media in

such a way as to discredit governmental agencies and physicians . . ."

In his paper "Controversies in Current Immunization Policy and Practices: One Physician's Viewpoint" (in Current Problems in Pediatrics 6: 3-35, 1976), Dr. Fulginiti had this to say about pertussis vaccine:

PERTUSSIS VACCINE--DOES IT WORK? IS IT SAFE?

> Despite more than 30 years of experience with pertussis immunization, the reasons for recovery from the acute infection and subsequent immunity are still uncertain. It is known that second attacks are rare following natural disease. It is also known that 45-95% of recipients of pertussis vaccine are susceptible to pertussis up to 12 years later. A variety of antibodies directed against the organism have been described but correlation with immunity is not perfect. Skin test reactivity has also been noted but no definite link to immunity has been determined. In short, we do not know why patients recover from pertussis, and we do not understand the immunologic mechanisms involved in resistance to infection after natural disease or immunization.
>
> Is pertussis vaccine effective? An examination of the history of the disease points out the difficulties in interpretation of efficacy. Prior to the widespread use of pertussis vaccine both the incidence of pertussis and the case-fatality ratio declined. A 50-fold reduction in incidence and an 84% reduction in case-fatality were recorded in Great Britain in the years between 1947 and 1972; the case-fatality ratio decreasing prior to the fall in incidence. These data suggest that pertussis virulence was declining before pertussis vaccine and that the incidence of the disease continued to fall, both before and after introduction of the vaccine. To further complicate the analysis, serial studies of pertussis vaccine efficacy have shown results varying from no effect through 20% protection to 80% protection. In general, the efficacy of a given vaccine was related to its potency, as determined by mouse-protective tests. In England, protection provided

by vaccines prior to 1968 was meager; no greater than 20% protection was noted. Since that time there have been changes in both the specific antigenic content and in total potency plus changes in the schedule of vaccine administration. Presumably, these changes will provide greater efficacy, but this premise has not been validated yet. A running correspondence in Lancet late in 1974 pits the critics of pertussis vaccine against its proponents. However, despite potent arguments on both sides of the issue, in the absence of controlled field trials the truth cannot be determined. Britain currently is in the peculiar position of advocating use of a vaccine for which there are no hard data in the face of mounting epidemics of pertussis. Between late 1973 and this writing in 1975, the incidence of pertussis had risen 7-fold over that recorded earlier. Critics of pertussis vaccine cite these data as evidence for the failure of pertussis immunization. Advocates of the vaccine point out that the current epidemic is primarily among unvaccinated children and fits the expected biyearly pattern of pertussis epidemics. The issue remains unresolved.

In the U.S. a vaccine is employed in the potency range of anticipated efficacy, but limited to that level of potency below which reasonable safety is expected. The issue of safety of pertussis vaccine is the genesis of the concern over efficacy. If the vaccine is associated with a high risk of reactions, then dubious efficacy would command its deletion from practice. If the vaccine is effective, an arbitrary decision as to allowable hazard must be made. The two issues are inexticably interwound. Hence, a consideration of the safety of pertussis vaccine follows.

The first serious adverse consequence of pertussis immunization was reported in 1933; Madsen describes a fatal convulsive episode in a 1-week old infant. Subsequently, numerous isolated reports have appeared linking pertussis immunization to adverse reactions, especially a post-vaccinal encephalopathy. Attempts have been made periodically to record all complications in a given group of patients in systematic fashion. The results are as divergent as those data recorded for efficacy. Strom in Sweden detailed 36 instances of significant neurologic disease post-pertussis vaccine among 215,000 recipients, an incidence of approximately 1:6,000. Immediately, his analysis was challenged and a reworking of

his data suggested to others a "true" incidence of 1:50,000. In other countries the estimates have varied from none to 1:100,000. Amazingly, we do not know the incidence in the U.S. despite the recommendation that every child receive the vaccine.

Other reported mishaps following pertussis immunization range from the trivial to sudden death. The total number of all reactions in one of the Medical Research Council studies was 70%. These included local and systemic reactions.

There are a number of factors which cloud even the most careful attempts at evaluating the safety of pertussis vaccine. First, the vaccine is administered to a group of infants at a time during which a large number of infections occur. This background, coupled with the occurrence of noninfectious diseases, renders uncertain an individual judgment linking reaction to vaccine. For example, the author was consulted on a 6-month-old child who had prolonged convulsions within 24 hours after a third dose of pertussis vaccine. The history and physical examination contributed little, but examination of the spinal fluid yielded a moderate pleocytosis. An echo-9 virus was recovered from the throat and stool and a 4-fold increase in antibody detected over a 3-week period. How does one judge this incident in relation to pertussis vaccine? Is it unrelated? Is it an instance of pertussis encephalopathy with coincidental echovirus infection? Is it both? Did the pertussis vaccine permit central nervous system infection with the enterovirus? By present methodology, these possibilities cannot be sorted out. And yet, instances similar to the above occur frequently.

A second confusing factor is the time relationship between vaccine administration and adverse event. How long an interval is possible in a vaccine-induced central nervous system infection or other untoward effect? Strom recorded data on some patients who first fell ill with neurologic symptoms 1 week after receipt of vaccine. Is that disease relatable to the vaccine? Most experts accept an interval of 24 hours between vaccine and onset of encephalopathy; a few suggest 2-3 days as an acceptable delay in onset. But there is no proof for any interval. In fact, the very nature of postpertussis encephalopatny is not clear, even in infants who have died. In a patient who survives such an episode there are

no certain diagnostic tests which link pertussis vaccine and observed neurologic disease. It is little wonder that confusion exists as to the incidence of this complication!

SUMMARY AND ANALYSIS

Pertussis vaccine is presumed to be effective based on a limited number of trials and extrapolation from experience. Its safety is questionable; the exact incidence of side-effects is not known with certainty, with the best estimates for all adverse consequences at 70%, and for central nervous system sequelae somewhere between 1:6,000 and 1:100,000 doses of vaccine.

For the present, evidence for efficacy of the current vaccine suggests that it provides protection of a substantial, but not absolute or even ideal, degree.

Safety is equivocal. If the higher estimates of serious central nervous system and other sequelae were to be substantiated, the vaccine should be withdrawn in light of its less than ideal efficacy. Uncontrolled experience and common sense seems to indicate that serious pertussis vaccine complications are infrequent, or are attributable, in part, to other causes. The absence of adequate field data makes such assumptions feeble, if confronted with a single patient with a compatible complication.

To me, it is inconceivable that we can steadfastly recommend and employ pertussis vaccine without a parallel commitment to resolve the outstanding issues. It is my belief that the National Institutes of Health, the Food and Drug Administration and CDC should constantly encourage competent authorities to investigate the unanswered questions and attempt definitive answers. Specifically the following should be accomplished:

1. Attempts should be made to identify the specific immune mechanisms operative in recovery from and immunity to pertussis.
2. Investigation of the precise incidence of local and systemic complications of pertussis vaccine should be undertaken.
3. Field trials, in areas of high pertussis endemnicity, should be carried out to evaluate the efficacy of pertussis vaccine in protection against disease.

> Some have also called for investigation of the potential role of pertussis immunization among individuals older than 6 years of age. It is my belief that such studies are premature and may detract from the resources and manpower needed to accomplish the primary objectives listed above.
>
> Pertussis is still a potentially devastating disease. Protection against pertussis is needed and wanted. Abandonment of pertussis immunization, in the face of reasonable assertion of its protective effect, would be irresponsible. Uncertainty as to its safety is unwarranted in the light of our current scientific capacity. Complacency in acceptance of the equivocal status quo is intolerable and should not continue.

In his testimony Dr. Fulginiti failed to say what occurred in the interval 1976-1982 that resulted in less uncertainty as to the safety of pertussis vaccine: In 1976 he found "Uncertainty as to its safety is unwarranted in the light of our current scientific capacity. Complacency in acceptance of the equivocal status quo is intolerable and should not continue."

It is noted here that Dr. Fulginiti testified that "The American Academy of Pediatrics has long favored a Vaccine Compensation System and is actively promoting this concept with various branches of the federal government . . ."

Dr. Robert Parrott and Dr. Shirley Fannin. The theme of a "Vaccine Compensation System" introduced by Dr. Fulginiti was carried forward by Dr. Parrott in his testimony. Dr. Parrott said that "In the rare instance

where a neurological complication apparently occurs [following vaccination], the family can undergo considerable financial burden and in despair sue the physician or manufacturer for liability. A 'Workman's Compensation-like' recompense would be more just and appropriate to the situation."

Dr. Fannin had a more inclusive solution to "the problem." She said "If you ask me how to solve the problem, I can only suggest more funding for immunization from the state and Federal government."

In my judgement, the thrust of the testimony given by Drs. Foege, Fulginiti, Parrott and Fannin before the Subcommittee at this Hearing on immunization and preventive medicine was either misleading, self-serving or both and careful efforts by the public to understand the thrust of their statements will only erode further the public's confidence in vaccines.

It is clear, at least to me, that the issues before the Subcommittee at this Hearing were not presented to the public clearly and accurately and til they are the complacency and uncertainty that were found in 1976 by Dr. Fulginiti to be unwarranted, unacceptable and intolerable will continue on into the future and legislation to establish a "Vaccine Compensation System" (Fulginiti) or to provide "more funding for immunization

from the state and federal government" (Fannin) will make it possible for those who caused the problems to escape responsibility through the proposed vaccine compensation system and to cause more problems with requested additional funding.

Study of the Foege, Fulginiti, Parrott and Fannin statements served a useful purpose: their study emphasized the fact that it is now 10 years since Senator Abe Ribicoff held Hearings on 2 May 1972 before the Subcommittee on Executive Reorganization and Government Research (92nd Congress, 2nd session on Titles I and II of S.3419) concerned with vaccine regulation and vaccine use in this country.

Study of the 7 May 1982 Hearing statements gave to me clear and convincing evidence that it is now time to reexamine vaccine regulations and vaccine use in this country. The 7 May 1982 Hearing, I hope, is the first step in this reexamination.

Senator Hawkins. Thank you.
[Whereupon, at 12:40 p.m., the subcommittee was adjourned.]

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DEPARTMENT OF COMMUNITY MEDICINE

20th August 1982

Senator Paula Hawkins,
US Senate,
Washington DC, 20510.

For the attention of Mr. Jay Howell

Dear Senator Hawkins,

Pertussis Vaccine

Colleagues in America have sent me copies of statements and testimony before the Sub-committee on Investigations and General Oversight of the Committee on Labor and Human Resources of the United States Senate on May 7th 1982. These include a testimony by Dr. Vincent A. Fulginiti on behalf of the American Academy of Pediatrics and Dr. William H. Foege, Director of the Center for Disease Control and it is with regard to their statements that I am writing to you because they both refer to me by name. Dr. Fulginiti misquotes my data and misinterprets my views on pages 5 and 6 of his testimony. Dr. Foege quotes me correctly but incompletely on page 10 of his statement but accuses me wrongly on page 14 of attributing encephalopathy to pertussis vaccine without investigating other possible causes. The figures which he quotes in this regard are erroneous, although the estimate given of the frequency of encephalopathy is that which I calculated. Both he and Dr. Fulginiti refer only to one short publication by me in 1977, overlooking or ignoring other relevant studies published subsequently in Britain and in the United States.

Reference is also made to the programme by NBC/WRC TV broadcast in various parts of America, in which I appeared. It is alleged that this programme is "distorted, verging on the irresponsible" (Dr. Foege) and "biased and inaccurate" (Dr. Fulginiti). I have to say that I met with the television staff responsible for the programme on four occasions. There was no pressure upon me in any way to give anything other than my own personal opinion. They made every effort, as far as I was concerned, to examine an impressive volume of evidence and to research and present both sides of the case. Having seen the programme, I think it is unfair to accuse them of bias and sensationalism and to allege, as Dr. Foege does, that "attempts are being made to provoke a major controversy where one does not currently exist".

The testimonies to which I refer are by distinguished physicians representing organisations for which, from personal knowledge as well as repute, I have great respect. I regret having to raise objections but I can provide chapter and verse to support them if you so desire.

Yours sincerely,

Gordon T. Stewart.